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EVALUATION, PREVENTION AND SURGICAL TREATMENT OF POST-KERATOPLASTY ASTIGMATISM WITH THE USE OF COMPUTER ASSISTED VIDEOKERATOGRAPHY

by

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ABSTRACT

Astigmatism is a common complication after penetrating keratoplasty (PKP) that affects visual rehabilitation in a considerable number of patients. The scope of this thesis was to investigate different aspects of problem "post-PKP astigmatism" with the aid of computer assisted video-keratography (CAVK) through four parallel studies.

First, the agreement and repeatability of CAVK were evaluated against the keratometer. A systematic bias of CAVK in measuring steeper principle meridians and higher amount of astigmatism on normal corneas was demonstrated. Measuring agreement between the two instruments on post-PKP corneas was worse than in normal corneas. CAVK repeatability was also found to be observer related as well as astigmatism related. A novice observer has shown larger variability in measurement, and higher deviation scores were seen for highly astigmatic corneas. Repeatability of keratometer measurements was found to be better for post-PKP corneas. The two instruments demonstrated clinically significant differences, both on normal and astigmatic corneas. It is concluded that they cannot be used interchangeably.

A new qualitative classification system is proposed in this thesis, for post-PKP corneas. Twelve distinct topographic maps were recognised and some of these may form a continuum. The interobserver repeatability was tested to be high (91% after second review), a prerequisite for any potential clinical application. In post-PKP corneas, the incidence of irregular astigmatism was found to be about double that of regular astigmatism (59% vs. 30% respectively), with prolate and oblate patterns seen in equal proportions (21%). Regular astigmatic patterns were found to be associated with higher astigmatism. Following PKP, the healing process and suture manipulations cause a decrease of the regular astigmatic patterns (and a corresponding increase of the irregular astigmatic patterns) with time.

In a prospective randomised study of 95 eyes, it was demonstrated with the aid of CAVK, that suture induced post-PKP astigmatism is not significantly different between a technique using a single continuous adjustable suture (SCAS) and a technique using a combination of interrupted and continuous sutures (ICS). Although SCAS offered an earlier visual stabilisation following PKP, it was also found to be associated with higher complication rates, in particular early loosening of the suture.

In the final part of this study, a prospective randomised study of 31 eyes was conducted to assess the advantage of CAVK (as compared to keratometry) in planning asymmetric surgery with relaxing incisions and compression sutures for the surgical correction of high post-PKP astigmatism. The improvement in the results was found to be limited when CAVK was used, but this may be due to the fact that most of these corneas showed regular astigmatism preoperatively.

To the holy memory of my father...

Στην ιερή μνήμη του πατέρα μου....

" TOPOGRAPHY

[Greek : *topos* (τοπος) = location + *graphein* (γραφη) = to write]

The description of an anatomical region or of a special part "

" KERATOGRAPHY

[Greek : *kerato* (κερατοειδης) = cornea + *graphein* (γραφη) = to write]

The description of the cornea"

" ASTIGMATISM

[Greek : *a* - neg. + *stigma* (στιγμα) = point]

Unequal curvature of the refractive surfaces of the eye; hence a point source of light cannot be brought to a point focus on the retina but is spread over a more or less diffuse area "

Dorland's Medical Dictionary

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AUTHOR'S DECLARATION

This is to certify that all work presented in this thesis was the result of personal observations by the author, unless fully acknowledged otherwise. This thesis does not incorporate any material previously submitted for a degree or diploma in any university. The views expressed in this thesis are those of the author and do not necessarily reflect those of the University of Bristol.

20 September, 1997

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ABBREVIATIONS APPEARING IN THE TEXT

A	Angstrom
ABK	Aphakic bullous keratopathy
ANOVA	Analysis of variance
BCVA	Best Corrected Visual Acuity
CAVK	Computer assisted Videokeratography
CS	Compression Sutures
CCD	Charge Coupled Device
CL	Contact lenses
CMS	Corneal Modelling System
CTFS	Corneal Transplant Follow up Study
D	Diopter
ECCE	Extracapsular cataract extraction
F/S	Flattening / steepening (coupling) ratio
GAG	Glycosoaminoglycans
HSK	Herpes Simplex Keratitis
IC	Interrupted and continuous (suturing technique)
IOL	Intraocular lens
IOP	Intraocular pressure
K2	Surgical effect
K2'	Net surgical effect in ideal axis
LS	Localized Steep pattern
LSUCTS	Luisiana State University Corneal Topography System
mink	Minimum keratoscope reading
mm	millimetre (1 mm = 10^{-3} m)
µm	micrometer (1 µm = 10^{-3} mm)
nm	nanometer (1 nm = 10^{-9} meter)
OABT	Oblate Asymmetric Bow Tie pattern
OI	Oblate Irregular pattern

OSBT	Oblate Symmetric Bow Tie pattern
PABT	Prolate Asymmetric Bow Tie pattern
PAS	Periodic acid-Schiff
PBK	Pseudophakic bullous keratopathy
PHMB	Polyhexamethylene biguanide
PI	Prolate Irregular pattern
PKP	Penetrating keratoplasty
PMMA	Polymethylmethacrylate
PRK	Photorefractive keratectomy
PSBT	Prolate Symmetric Bow Tie pattern
PVA	Potential Visual Acuity
RGP	Rigid gas permeable contact lenses
RK	Radial keratotomy
RxI	Relaxing incision (keratotomy)
SA	Surgical accuracy
SAI	Surface Asymmetry Index
SCAS	Single continuous adjustable suture
SD	Standard deviation
SE /SEM	Standard error of the mean
SF	Steep Flat pattern
SRI	Surface Regularity Index
simk	Simulated keratometry reading
TKP	Thermokeratoplasty
TMS-1	Topographic Monitoring System-1
UKTSSA	United Kingdom Transplant Support Service Authority
VA	Visual acuity
VKS	Videokeratography system
VPU	Video processing unit

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CHAPTER 1

GENERAL INTRODUCTION

1.1. THE CORNEA - GENERAL CONSIDERATIONS

1.1.1. Structure of the cornea

The cornea forms the anterior transparent one-sixth of the eyeball. When seen from the front, it is convex but somewhat elliptical in shape, with an approximate vertical diameter of 10.6 mm, but about 11.7 mm horizontal diameter in adults. However these dimensions vary considerably between individuals. On the posterior surface the cornea is concave but circular with an average diameter of about 11.7 mm both vertically and horizontally. The cornea is thinnest in its centre, measuring about 0.5 to 0.6 mm (average approximately 525 μm) and thickens gradually at a rate of approximately 20 μm per 0.50 mm of radius from the centre approaching at the periphery, where it measures about 1.0 to 1.2 mm.

1.1.2. Microscopic anatomy of the cornea

Microscopically, the human cornea is an avascular structure composed of six layers. From outer to inner ocular surface, these layers are : the epithelium, the basement membrane, Bowman's layer, the substantia propria or stroma, Descemet's membrane, and the endothelium. Closely associated with the anterior corneal surface, is the tear film.

Epithelium : The corneal epithelium is stratified, consisting of five to six layers of nucleated cells; it measures about 50 to 70 μm. The most superficial cells are flat, squamous non keratinized, with tight junctions between them, showing on their outer surface microvilli which assist in retaining the tear film and increase the surface area for metabolic exchange. The middle or wing cells form two to three layers of cells in an intermediate state of differentiation. The monolayer of the cuboidal basal cells is the source of new cells for the corneal epithelium. These cells are attached to the underlying basement membrane with hemidesmosomes.

Basement membrane (basal lamina) : This is an adhesion complex with a thickness of 20 to 30 nm. It is consisted of anchoring fibrils and plaques of type

VI and VII collagen (*Sakai et al,* 1986; *Marshall et al,* 1991) trapped in the meshwork of collagen fibrils in the underlying Bowman's layer (*Keene et al,* 1987). This layer is not visible by light microscopy and stains positive with periodic acid-Schiff (PAS).

Bowman's layer : This is an acellular transparent layer of about 8 to 12 μm thickness, lying immediately beneath the basement membrane of the epithelium. It is distinct in light microscopy but without definite structure, whereas with electron microscopy it loses its identity and appears as a group of irregularly arranged collagen fibrils of type V and VI (*Marshall et al,* 1991) embedded in intercellular substance. Bowman's layer is relatively resistant to trauma; it shows no regenerative ability when injured.

Substantia propria or stroma : This is the thick central layer forming about 90% of the whole corneal thickness (500 μm centrally). It is composed of many lamellae of collagen fibrils with glycosoaminoglycans (GAG, extracellular matrix) filling the interstitial surfaces. The collagen lamellae are nearly parallel to the corneal surface and each is about 2 μm thick. The collagen fibers are approximately 25 nm in diameter and show a spacing of 64 nm between them. Their direction in each lamella is the same, but they run at right angles to the lamellae of adjacent layers. This specialised arrangement of the fibrils accounts for the optic uniformity of the cornea. The collagen of the lamellae is predominantly of type I with type III and V also present (*Nakayasu et al,* 1986). The GAGs that represent the polyanionic extracellular matrix, are keratan and chondroitin sulphate. They are important in the regulation of the water content of the tissue and hence its transparency. Between lamellae, flattened fibroblasts called keratocytes are found. These cells have a large nucleus and many processes. Other cells including macrophages, lymphocytes and polymorphonuclear cells are also occasionally seen.

Descemet's membrane : This layer lies on the posterior surface of the stroma and represents the thick basal lamina secreted by the corneal endothelial cells. It is composed of fine type IV collagen fibres (*Nakayasu et al,* 1986) and has a thickness of about 10 μm. It can be divided into an anterior striated part produced during gestation and a posterior amorphous non-banded layer with high elasticity which thickens throughout life.

Endothelium : The corneal endothelium measures approximately 3μm (*Feuk & McQueen,* 1971) and is a monolayer of flattened hexagonal cells of mesenchymal origin lining Descemet's membrane. Their inner surface is bathed by the aqueous humor. They show interdigitations and tight junctions with one another and a few microvilli on their free surface. These cells play a major role in the control of the corneal hydration by an active transport mechanism and by limiting the access of water from the aqueous humor. Although incapable of mitotic activity, they have the ability to enlarge. Their normal density in the adult eye is 1400 to 2500 cells/mm^2, declining with age. When their number falls below 800 cells/mm^2 (critical density) the endothelial function fails, resulting in corneal oedema (*Forrester et al,* 1996).

1.1.3. Corneal transparency

The cornea functions both as a window and as the principle refractive surface of the eye and so it must combine optical clarity and structural stability in order to produce a sharp image to the retinal photoreceptors.

Maurice (1957), proposed the crystalline lattice theory for the explanation of the corneal transparency, based on the principles of geometrical optics. According to this, the striated fibrils within the corneal stroma show a uniform diameter and are distributed in a completely regular interfibrillar distance throughout the lamellae, forming lattice structure. Despite the disparity between the refractive index of dry collagen (n=1.550) and the stromal ground substance (n=1.354), the corneal stroma scatters less than 10% of the incident light (*Feuk & McQueen,* 1971). This is because the lattice arrangement of the collagen fibrils causes scattering of light to be eliminated by destructive interference from individual fibrils (*Maurice,* 1957). When the distance between fibrils is less than a wavelength of light, the cornea remains transparent, whereas whenever it is greater, destructive interference no longer occurs and the cornea appears hazy due to scattering of the light. However later studies, based on the theory of diffraction of light indicate that significant light scattering occurs only when regional fluctuations in refractive index exceed a critical dimension equal to one half the wavelength of light (2000 A) (*Goldman et al*, 1968). Thus the absence of corneal transparency is not a consequence of absent lattice arrangement, but rather a variation in the fibrils diameter or ground substance which results in different refractive index of the region.

Among other anatomical and physiological factors involved in the transparency of the cornea, are: *i)* the uniformity and regularity in arrangement of the epithelial cells. These are tightly packed together, so that almost no extracellular water is found in this layer and therefore no fluctuation in refractive index occurs *ii)* the absence of blood vessels, *iii)* the mechanisms that keep the cornea in a relative dehydrated state, such as the active metabolic pump of the endothelial cells for water, sodium and other electrolytes, the anatomic integrity of both endothelium and epithelium, and the evaporation of water through the anterior surface.

1.2. THE CORNEA AS A REFRACTIVE MEDIUM

1.2.1. The cornea as a spherical refractive surface

The anterior corneal surface or more precisely the air-tear interface is the major refractive element of the eye. This was first demonstrated by the early work of *Hermann von Helmholtz* (1821-1894) who invented the ophthalmoscope and refined the ophthalmometer. *Gullstrand* (1924) developed the most authoritative schematic eye model based on Helmholtz's schematic eye. Gullstrand using the photokeratoscope and the slit lamp that he invented, was able to make *in vivo* measurements of the corneal contour and thickness.

In the classic optometrical literature Gullstrand's relaxed schematic model eye has been accepted as the best representation of the optics of the eye. According to this model there are simplified calculations that can be performed for the cornea, taking in consideration the following assumptions: *i)* the geometrical theory of image formation as this is applied to refraction by curved surfaces. *ii)* the cornea is considered as a perfect curved surface, part of a spherical surface of a certain radius of curvature (R), and its power is determined by its radius of curvature. A shorter radius of curvature of a spherical surface creates a steeper arc and greater refractive power, and conversely a longer radius of curvature creates a flatter arc and less refractive power [Appendix I]). *iii)* the cornea can also be regarded as a thin lens with two refracting surfaces, one with positive power P_1 (anterior surface) and one with negative power P_2 (posterior surface) both of which affect its total power P_t according to the equation $P_t=P_1+P_2$. *iv)* by knowing the radius of curvature of the cornea, the power can then be calculated from the equation $P = n_1 - n_2 / R$ (n_1 and n_2 are the refractive indices for the two media, with values: 1 for the air, 1.376 for the cornea, 1.336 for the aqueous; R is the radius of curvature in meters; Table 1.1).

1.2.2. Refractive power of the normal cornea

As early as 1924, *Gullstrand* had reported quantitative data of normal corneal contour using the keratometer. According to his measurements in 220 adult male eyes and 92 adult female ones, the mean central corneal curvature was 7.858 mm for males and 7.799 mm for females. Similar results have been reported since, with mean values ranging from 7.51 mm (*Daily & Coe,* 1962) to 7.80 mm (*Stenstrom,* 1948). The last mentioned reference cited by *Clark* (1974), is one of the most extensive conducted studies and included over 30,000 patients.

The refractive power of the cornea is determined by both the anterior and posterior curvatures. Based on Gullstrand's data, for radius of curvature of 7.7 mm for the anterior corneal surface and 6.8 mm for the posterior one, the cornea contributes 43.1 D of the refractive power, compared to the total 58.6 D for the

TABLE 1.1 : Optical constants of the eye [*Gullstrand,* 1924]

	Average	Range
Refractive index		
Air	1.000	
Cornea	1.376	
Aqueous	1.336	
Lens	1.386 - 1.402	
Radius of curvature		
Anterior corneal surface	7.7 mm	7.1 - 8.4 mm
Posterior corneal surface	6.8 mm	
Dioptric power*		
Anterior corneal surface	48.8 D	
Posterior corneal surface	- 5.9 D	
Net corneal power	43.1 D	39 - 48 D
Net lens power	19 D	
Total power of the eye	58.6 D	

* after *Listing,* 1853 reduced eye calculations

whole eye. The anterior corneal surface accounts for 48.8 D and the posterior one -5.9 D. The posterior corneal surface has a negative power because the light diverges as it passes through a convex surface from a higher to a lower refractive index medium. Thus, the anterior corneal surface contributes about 83% of the total refractive power of the relaxed eye. When accommodation is involved, this proportion falls to 69% for a near focusing point at 92 mm in front of the front corneal vertex (*Kiely et al,* 1982).

1.2.3. Corneal asphericity - the cornea as an elliptical surface

Although the central corneal radius of curvature has been studied for a long period, the concept of corneal asphericity has been studied in depth only in relatively recent years, mainly due to the later use of improved methods in measuring corneal contour.

It is an oversimplification when making calculations to consider the cornea as part of a regular spherical surface, as its actual shape is quite variable, and generally speaking the normal anterior corneal surface is *asymmetrically aspherical.* In an aspherical surface the radii of curvatures vary continuously with distance from the centre to the periphery, while a spherical surface has only one radius of curvature. Aspherical surfaces are generally the result of surfaces produced by rotation of a conic section in directions other than parallel with the base of the cone (*Benjamin & Rosenblum,* 1992) and are also called conicoidal surfaces. An ellipse is an example of a conicoidal surface. A useful simplification to understand the topography of the cornea is to consider its curvature as a section of an ellipse [Appendix I, II].

The corneal asphericity was noticed quite early. In 1846, Senff measuring three meridians in two eyes recognised a peripheral flattening of the cornea (*Stone,* 1962). He showed that the cornea deviates from a sphere and is better approximated by an elliptical surface. Later, *Helmholtz* (1924) made his own measurements on three female eyes that resulted in exactly the same findings as Senff. He described these corneas as resembling an approximate *prolate ellipsoid.* In a prolate ellipsoid the curvature from the centre to the paracentral areas is changing from steeper to flatter. The type of curve resulting from the profile of such a cornea is called *hyperbole* [Appendix I]. This configuration in mathematics is described as having a positive shape factor [Appendix II].

Thus, the classical ophthalmic literature is in general agreement that the cornea is typically steepest centrally with progressive flattening towards the periphery and that the central corneal dioptric power is quite variable. This structure of the anterior corneal surface results in a positive aspherical lens surface, which reduces both oblique astigmatism and spherical aberrations (*Born & Wolf,* 1959).

Mandell (1962), also demonstrated that the normal cornea is aspheric and flattens from the centre to the periphery. Although there are earlier studies suggesting that normal human corneas are not always steeper centrally and flatter peripherally (*Clark,* 1973a; *Kiely et al,* 1982; *Cohen et al,* 1984), this concept following recent studies is no longer accepted. In contrast to those findings, *Bogan et al.* (1990), using videokeratography (*vide infra*), found that all normal corneas are steeper centrally and flattened paracentrally and peripherally, that is they have a prolate shape and a positive shape factor. The difference between the central and peripheral steepness of the cornea may be as much as 4 to 5 D in some cases. The nasal cornea is flatter than the temporal cornea (*Gullstrand,* 1924; *Knoll,* 1961; *Clark,* 1974). In another study (*Dingeldein & Klyce,* 1989) performed on 44 normal corneas, the most striking finding was the high degree of mirror image symmetry (enantiomorphism) often found between the right and left eyes.

1.2.4. Corneal surface zones

In a qualitative method to describe corneal contour, the cornea is said to consist of different surface zones. *Aubert* (1885), first proposed that the normal cornea can be divided in two zones; a central spherical zone and a peripheral zone of gradual flattening. The central zone is 3 to 4 mm in diameter and approximates a sphere of nearly "constant radius of curvature". So, conventionally there are four concentric anatomical zones that are recognised and defined artificially (*Waring,* 1989a).

Central zone **:** This measures approximately 4 mm in diameter. Optically it is the most important zone of the cornea as it serves as a refracting surface for central vision (*Morrow & Stein,* 1992).

Paracentral zone : This is an annulus approximately 4 to 7 mm in diameter and represents the 'intermediate' part of the cornea. Normally, this zone has a flatter radius of curvature than the central zone. Together with the central zone, the two zones represent what is called the *apical zone or corneal cap.*

Peripheral zone : This also called transitional zone, is an annulus of 7 to 11 mm in diameter. It is the area where the normal cornea shows the maximum flattening and asphericity with an increasingly longer radius of curvature.

Limbal zone : This is the rim of cornea approximately 0.5 mm wide, covered by the limbal vascular arcade. Here a focal steepening occurs.

However, as it has been shown in more recent studies (*Dingeldein & Klyce,* 1989; *Bogan et al,* 1990), none of these areas is discrete and it is anatomically incorrect to divide the cornea into zones. The corneal cap itself does not have a constant radius of curvature, but rather a radius of curvature that begins to change immediately when moving away from the apex, but at a slower rate than the corneal periphery (*Mandell,* 1992). The optical zone forms the foveal image through the entrance pupil of the eye; its size, shape and curvature vary among individuals. The mid and peripheral cornea serves three purposes according to *Miller & Carter* (1988): *i)* a refractive surface for peripheral vision and the foveal image when the pupil is widely dilated, *ii)* a mechanical support structure to sustain the curvature of the central cornea and *iii)* a source of epithelial cells, keratocytes and endothelial cells during normal turnover and repair.

1.2.5. Mathematical models for representation of the corneal shape

The complex shape of the cornea is difficult to understand and measure mathematically and also difficult to represent graphically and treat optically. Although this is an oversimplification, it is possible to fit almost any radius data from any single corneal semi-meridian very closely to an elliptical curve and for the optical part of the cornea the elliptical model is adequate (*Mandell & St Helen,* 1971). The situation however changes at the corneal periphery, because there the rate of flattening exceeds that of an ellipse. When the conicoid representation of the cornea is extended towards the limbus, conicoids cannot adequately describe the rapid change in corneal shape and cannot measure correctly the radius of curvature at the periphery (*Kiely et al,* 1982).

Different logarithmic mathematical representations of the corneal shape have been proposed (*Baker,* 1943; *Bonnet & Cochet,* 1962; *Lotmar,* 1971; *Guillon et al,* 1986). In general, two mathematical models have been advanced to simulate the corneal shape: the mean ellipsotoric model and the sinusoidal arc model (*Burek & Douthwaite,* 1993).

There are a number of mathematical algorithms and ray-tracing programs that have been devised to reconstruct the corneal surface. The point-to-point method in which the values of radius of curvature or power at different positions on the corneal surface are measured and the array is calculated (*Klyce,* 1984) is used by most of the modern videokeratography equipment (*vide infra,* section 1.3.5.5).

1.2.6. Variations in corneal shape

The corneal contour is subject to measurable changes under certain conditions. With the exception of factors such as ageing and mechanical pressure, the evidence presented in the literature for some alleged effects such as convergence, accommodation, or the use of atropine or pilocarpine, is usually of doubtful validity and probably within the accuracy limits of the instruments used (*Clark,* 1973a). However it appears that whenever an "unnatural" agent, such as external ocular pressure, acts against the cornea for a brief time, the corneal shape will recover in a matter of hours or minutes. Whenever forces are maintained for much more prolonged time e.g. the theory of lid pressure as a factor in the aetiology of with-the-rule astigmatism, or contact lenses wear, the effects are probably more prolonged (*Knoll,* 1976). The cornea is thickened overnight by about 3 to 8%, but returns to normal within 2 hours of lid opening. Hypoxia rather than lid closure is believed to cause corneal swelling during sleep (*Kiely et al,* 1982; *Harper et al,* 1996).

1.3. METHODS FOR ASSESSMENT OF CORNEAL TOPOGRAPHY

1.3.1. Introduction - terminology

The term topography derives from the Greek "τοποϛ"-'place' and "γραφη"-'write'. Although topography literally means to write about a place, it also means to describe a location. In ophthalmology the term is used when referring to the contour of the cornea as *corneal topography.* Thereafter assessing corneal topography means finding ways to measure the shape of the cornea and if possible present our findings in comprehensive terms.

At present all that we can measure is the anterior curvature of the cornea, or more accurately the air-tear film interface, although clinically we usually want to know the power of the cornea.

1.3.2. Keratometer (Ophthalmometer)

This is an instrument used routinely for the measurement of the corneal shape. In principle the keratometer measures the central corneal curvature only, from the reflection of mires from four points along two meridians at right angles on an annulus 3 to 4 mm in diameter. There are several types of these instruments available today, but essentially all are modern refinements of two old designs one by von Helmholtz and the other by Javal and Schiotz.

1.3.2.1. *History*

In 1856, *von Helmholtz* constructed the ophthalmometer based on a design made by Jesse Ramsden in 1796 (*Mandell,* 1960). This device enabled him to determine the central corneal curvature. Helmholtz with his ophthalmometer also measured the peripheral cornea and deduced that the cornea was approximating an ellipse (*Mandell,* 1960 and 1962). The term "keratometer" is the commercial name for the same instrument manufactured by Bausch & Lomb Inc. (Rochester, NY), and has taken on a generic use.

In 1881 Javal and Schiotz constructed their own keratometer which in many respects is very similar to that of Helmholtz's earlier model. The main difference is that Javal and Schiotz employed the image of constant magnification and measured the size of the object necessary to produce it, whereas Helmholtz used an object of constant magnitude and arrived at the corneal curvature by measuring the reflected image. The Javal-Schiotz keratometer is more suitable for clinical practice and the Helmholtz's ophthalmometer for research purposes.

1.3.2.2. *Optical principles of keratometry*

The principle of keratometry is to determine the relationship between the size of an object (target) and the size of its virtual image formed by the cornea which acts as a convex mirror. From this relationship the unknown radius of corneal curvature can be then determined from optical formulas (*Mandell & St Helen,* 1971). The target projected from the keratometer is an illuminated mire 3 to 4 mm in diameter. After reflection to the anterior corneal surface, an image is formed which is virtual, smaller and erect located within the anterior chamber of the eye. This is illustrated in Appendix III.

Calculation of radius of curvature

Based on the theory of reflection for convex mirrors, the radius of curvature (R) can be measured according to the equation $R = 2\,U\,L\,/\,O$, where U = distance of an object, L = image size, O = object size [Appendix III]. This is known as the *keratometric formula.*; it assumes first order or paraxial theory which does not take into consideration aberrations which occur in reality and alter the size of the image. According to this formula, by measuring the size of the image formed (L), of an object of known size (O) and position (U), the radius of curvature (R) can be easily calculated. In practice, the object of known size is the distance between the two object mires of a keratometer, an illuminated mire 3 to 4 mm in diameter. The distance L between the two reflected points varies from approximately 2.6 to 3.7 mm depending on the corneal curvature (*Dabezies & Holladay,* 1984).

Calculation of corneal power

The keratometer directly measures the radius of curvature of the cornea. Most of the instruments however, are calibrated to give the corneal power value as well.

In order to achieve this an assumption must be made that the back surface of the cornea has a negative power of approximately one-tenth of the positive power of the front surface (*Stone,* 1975). Thereafter instead of calibrating the instrument to the true refractive index of the cornea (1.376), a lower modified refractive index is used.

Optics of the keratometer

Keratometers are short focus telescopes consisting of an illuminated unit and an observing unit. The illuminating unit consists of a light source, a mirror, a condensing lens and a target. The target is a circular disc with openings designed to create a specific configuration varying between different models. The refracted corneal image becomes an object refracted through the objective lens. The observing unit consists of an astronomical telescope (for magnification since the reflected image is only 3.2 mm), and a doubling system. The image formed by the objectives of the telescope must be viewed through the eyepiece. The optical system of the keratoscope must measure the separation of the two images (mires). As the reflected images from the anterior cornea are never quite stationary due to the fine fixation tremor of the eye, this measurement of separation distance is more easily carried out by using the doubling system. This system consists of two prisms interposed between the objective lens and its focal point. Each prism deviates the light resulting in two additional images, one horizontal and the other vertically oriented (*Dabezies & Holladay,* 1984).

The Helmholtz ophthalmometer incorporated a variable doubling device using glass plates. The image (mires) separation in this type of keratometer is fixed. The variable doubling is mechanically arranged so as to read off the radius of curvature directly. In the Javal instrument the doubling is fixed, the mires have variable separation, and this variable object size is used to measure the radius of curvature. Fixed doubling permits a simpler optical system than variable doubling. The Javal-Schiotz principle uses a Wollaston double image prism consisting of two rectangular quartz prisms cemented together (*Elkington & Frank,* 1991).

1.3.2.3. *Accuracy of the keratometer*

It has been commonly accepted that the keratometer has an accuracy of better than 0.25 D on measuring regular surfaces (*Wilson & Klyce,* 1991a). It has been shown both theoretically and experimentally (*Charman,* 1972) that diffraction of light sets a limit to the accuracy of the keratometer, and that this lower limit of reproducibility is about 0.2 D. In a clinical study, the range of repeatability for a keratometer (Bausch and Lomb) was found to be 0.75 D in the vertical meridian and 0.37 D in the horizontal meridian (*Brungardt,* 1969). In a review article on the values reported as the measurement error of commercial keratometers *Clark* (1973b), has pointed out that large discrepancies exist but there is a lack of statistical validation in the majority of the reported results and it is therefore impossible to make an unequivocal statement about the accuracy of modern keratoscopes. It was concluded that an estimate value of 0.015 mm in radius of curvature seems reasonable as the smallest error (SD) of conventional two mires keratometers for central corneal measurements. In a well designed study by *Tate et al* (1987), the accuracy of the Javal-Schiotz keratometer (Haag-Streit) as well as of two autokeratometers (Humphrey, Canon) was found to be within 0.37 D, with good correlation of measurements between the three instruments (0.8479 to 0.8880) in measuring normal corneas. The accuracy and repeatability for both instruments in measuring steel balls of known curvature was also demonstrated to be within 0.12D.

1.3.2.4. *Inaccuracies - disadvantages and advantages of keratometer*

The keratometer carries some disadvantages which are discussed below.

1) a limitation of keratometer is that it evaluates essentially only the central 3 mm of the corneal surface (*Rowsey et al,* 1981), representing only a very small fraction (about 7%) of the entire corneal surface (*Koch et al,* 1989).

2) the measurement of the keratometer is correct only when the surface measured is spherical or toroidal with the mires in the meridian planes of greatest or least curvature (*Clark*, 1973b). From Appendix III it is seen that the central corneal curvature is measured between two points. An assumption is made that the surface between these two points is spherical. Depending on the shape factor deviation of the surface measured from that of a sphere, errors can be induced in the measurements. Although having an accuracy of 0.25 D when the corneal surface is regular, the keratometer cannot measure irregular astigmatism or corneal asphericity (*Klyce & Wilson*, 1989). This is in fact the case for post surgical corneas. Furthermore accurate measurements by precise alignment of the mires is impossible in irregular ocular surfaces. 'One position' instruments in particular, tend to be quite incorrect for one of the two meridians because only one meridian can be at focus in toroidal corneas. Accuracy of the dioptric corneal power readings still depends on the type of scale provided (*Stone*, 1962), as the keratometric index used is based on values which are only assumptions (*Dabezies & Holladay*, 1984).

3) readings at the peripheral cornea are inaccurate due to the asphericity of the cornea outside the central area (*Guillon et al*, 1986; *Bonnet & Cochet*, 1962; *Mandell*, 1962). The major source of inaccuracies in peripheral keratometry is because the separation of the mire reflections is so large (3 to 3.5 mm). Measuring the peripheral cornea with conventional keratometry may lead to errors up to 3 D (*Mandell*, 1962).

4) the measurement of the keratometer is not performed at that part of the surface intersected by the instrument's optical axis, but rather at two widely separated parts of the surface (*Mandell*, 1962). It provides no information regarding the topography of the cornea within or outside the points of measurement. That means that there may be potentially wide variation of the corneal shape central and peripheral to the keratometrically measured points.

5) incorrect focusing of the eyepieces of the instrument produces inaccuracies. This can produce an error in the radius reading as much as 0.4 mm (*Stone,* 1962).

6) inaccuracies of mechanical nature (backlash) caused by the possible amount of freedom of movement of the control knob before it operates the movable mechanism of the instrument (*Stone,* 1975).

7) small errors occur in the calculation of the image reflection position, because the formula used to calculate the image size is not accurate for large size objects as the mires, due to spherical aberrations (*Mandell,* 1962).

8) observer's accommodation may cause small errors in measurements; to overcome this most instruments have an adjustable eyepiece with a graticule, or operate on a collimated optical system (*Stone,* 1975).

On the other hand the keratometer has the advantages of been accurate in normal corneas. The assumption of central spherocylindricity is an approximation of the reality for most corneal surfaces. This makes the keratometer a very useful device for contact lenses fitting on normal corneas. Difficult contact lenses fittings however, are facilitated by a knowledge of the peripheral corneal base curves and in that respect keratometry is inadequate. Other advantages of the instrument are its small size and it's relatively low price. It is easy to operate and provides rapid, quantitative and qualitative data (*Morrow & Stein,* 1992).

1.3.2.5. *Automated keratometry*

Since 1981 automated keratometers have been commercially available. The autokeratometer measures the corneal curvature both centrally and peripherally with three points of fixation. Infrared light is emitted to the cornea and is reflected to solid state detectors for analysis (*Dabezies & Holladay,* 1984). They carry the advantages of ease of use; less skill and time required for measurements (making it especially useful for use with children); and measuring a larger range of curvatures than manual keratometers (*Nakada et al,* 1984; *Jarvis et al,* 1987). Their disadvantage is the higher cost. In a large study (207 eyes), automated keratometry was found to be as accurate and reliable as conventional manual keratometry in measuring either normal or pathological corneas (*Jarvis et al,* 1987). However, in another study performed on 40 postkeratoplasty corneas and 50 corneas after radial keratotomy (*Binder,* 1989), standard and automated keratometry were found to produce significantly different results in determining both the amount and axis of astigmatism, with the difference in astigmatism measurement being statistically significant for the postkeratoplasty group. This contradicts the findings of *Jarvis et al.* (1987), on measurements of irregular corneas.

1.3.2.6. *Intraoperative keratometry*

The use of operative keratometry in order to provide better control of intraoperative factors contributing to postoperative astigmatism, was first introduced commercially by *Troutman et al.* (1977). Two types of surgical keratometers are currently available. i) Qualitative keratometers. These are not true keratometers, but rather intraoperative keratoscopes which produce a keratoscopic image of the cornea. The surgeon must then make a qualitative assessment of both the location and the degree of astigmatism by interpreting the distortion of the keratoscopic image. These keratometers have a poor accuracy of about ± 2.50 D. ii) Quantitative keratometers which measure the anterior corneal curvature and provide a readout to the surgeon. However, usually they do not identify the meridian of greatest corneal power as this depends upon subjective localisation by the surgeon. They have an accuracy of between 0.25 D to 0.50 D (*Frantz et al,* 1989).

1.3.3. Keratoscope

A keratoscope is an instrument that reflects a series of concentric circular rings to the anterior corneal surface. *Placido* (1880), the Portuguese oculist is recognised as the inventor of the hand-held keratoscope. The instrument consists essentially of a flat disc with painted homocentric alternating black and white rings on its surface [figure 1.1]. The reflections of the rings appear altered from the normal circular form if any astigmatism or other form of irregularity of the anterior corneal surface is present. So, in the case of astigmatism the rings will appear elliptical instead of circular. This very simple instrument has survived through the centuries almost in its original form, and has been the base for the development of many of the sophisticated instruments ophthalmologists use today. Although the keratoscope does not measure the cornea, it carries the advantage of supplying rapid, qualitative information regarding the anterior corneal contour. It can also assess the directions of the principal meridians of a toroidal cornea, and the corneal lustre or dullness, but its most important application is probably in the diagnosis of keratoconus by assessing the displacement of the corneal apex with respect to the visual axis. The keratoscope has the disadvantage of not detecting easily small degrees of corneal astigmatism. It also provides incorrect information if tilted, in which case the reflected image could be distorted even though the cornea is normal.

There are several modern versions of keratoscopes that follow the same principle of rings reflections for qualitative assessment of the corneal contour. Among them are the Klein keratoscope (Keeler Instruments Inc.), and the van Loehnen cylindrical keratoscope (JedMed Instrument Co.).

1.3.4. Photokeratoscopy

1.3.4.1. *History and principle of operation*

A photokeratoscope is simply a keratoscope mounted with a still camera behind the central hole of the target. A photograph of the reflected images can be taken. The target used is usually a Placido disc with concentric rings, but alternative targets such as hemispherical or cylindrical surfaces with rings of varying width

Figure 1.1 : Modern version of the hand held Placido disc.

In its original description, the disc measured 23 cm in diameter and at the centre of the disc there was a circular aperture with a hollow tube attached to it, through which the observer could look at the patient's eye. The main difference in the modern versions of the instrument compared to the original, is the use of an auxiliary magnifying lens in the keratoscope sight hole in order to magnify the reflected image.

The person to be examined should have his back to the light, fixate to the central hole of the disc, while care should be taken to raise the upper lid.

and spacing, have also been used (*Knoll,* 1961). The advantage of the latter designs is that they tend to correct the deficiency of flat targets in focusing simultaneously all rings in the camera system (*Mandell & St Helen,* 1971).

Photokeratoscopy has been used in the past by different investigators for qualitative study of the corneal contour (*Knoll,* 1961; *Ludlam & Wittenberg,* 1966) by observing the spacing and distortion of the rings. The rings appear closer together at steep areas, and further apart at places where the cornea becomes flatter. Additionally the mires become elliptical in the case of regular astigmatism, with the long axis of the ellipse corresponding to the meridian of the corneal flattening. In case of irregular astigmatism a distortion of the mires is observed, but not in an elliptical form. *Mandell & St Helen* (1971), using a photokeratoscope with an aspherical target measured the corneal contours of 8 subjects and tested various simple mathematical curves as possible models of corneal contour. They found that the ellipse, and in particular the hyperbola is an adequate approximation of the central cornea and that the change in radius for the corneal periphery is slightly higher than that of an ellipse. Quantitative measurements of corneal surface power based upon analysis of the shape of the photokeratoscope mires were only attempted relatively recently (*Rowsey et al,* 1981; *Doss et al,* 1981; *Rowsey,* 1983; *Rowsey & Isaac,* 1983) and this created a new interest in corneal topography and the evolution of new techniques. *Rowsey et al.* (1981), using the Corneascope evaluated the topography of 500 normal corneas, and 827 patients with keratoconus over a period of 8 years. They introduced a comparator that matched rings of the photokeratograph to reference rings of known diameter spheres. Their photokeratoscope provided colour or black and white Polaroid photographic images at a 4.8x magnification. Radius of curvature and consequently dioptric power were available by calculating the amount of magnification that the photographs would need to match corresponding standard comparator rings.

Doss et al. (1981), developed the use of a computational technique (algorithms) based on the raw data obtained by the corneascope to transform keratoscopic photographs into power diagrams giving corneal surface power at multiple points. Initially the corneal profile is reconstructed according to a multiple-arc technique and assuming that the cornea is spherical. The semi-chord length is compared to known calibration sphere tables in order to determine the corneal curvature. Then by applying a ray technique the optical power at each ring reflection is calculated.

1.3.4.2. *The step forward : Computer assisted photokeratoscopy - the LSU Corneal Topography System (LSUCTS)*

To overcome the deficiencies of photokeratoscopy, *Klyce* (1984) introduced a computer-based analysis system of the photokeratoscope images, extending and improving the work of *Doss et al.* (1981). This system was developed at the Louisiana State University (LSU), and proved to be the pioneer device for all future corneal topography analysis systems. It used the image from an 11-ring Nidek PKS 1000 photokeratoscope. After 5x photographic enlargement, the image was digitised with the HIPAD (Houston Instruments, Austin, TX) manual digitising equipment (*Klyce,* 1984; *Wilson & Klyce,* 1991a). Entering then the digitised image into a computer, statistical computing procedures were used to eliminate errors introduced by the digitisation process. The mire coordinates were subsequently transformed into three dimensional coordinates of corneal shape, from which point powers were calculated for 180 corneal meridians (*Dingeldein & Klyce,* 1988). Information however from the central and far periphery cornea could not be obtained, because as with other photokeratoscopes, the PKS 1000 mires did not cover these areas (*Maguire et al,* 1987a).

The presentation of the topographic information obtained by the LSU Corneal Topography System (LSUCTS) included initially a three dimensional wire model of corneal reconstruction, and a plot of dioptric point surface powers (*Klyce,* 1984). Later, the LSU Eye Centre further developed a graphic representation method in the form of colour coded maps (*Maguire et al,* 1987a). This provided the examiner with an easily understood image, unlike the numerical power plot.

1.3.4.3. *Advantages and disadvantages of photokeratoscopy*

Compared to the keratometer, the major advantage of the photokeratoscope is that it provides information from a larger portion of the corneal surface -55% of the total corneal curvature compared with 8% of the keratometer- (*Rowsey et al,* 1981). However the commercially available instruments provided limited information on the central cornea due to the instrument design constraints (*Wilson & Klyce,* 1991a). This is quite important as this is the most significant optical region of the cornea. Photokeratoscopy can give some quantitative evaluation of the corneal contour, but carries the disadvantages of induced aberrations and requirement of experience for the acquisition of good quality pictures (*Rowsey et al,* 1981). Another disadvantage is that the method of matching the photographs to the comparator screen implies a great deal of training and even topography experts cannot detect low amplitude or complex corneal surface distortions (*Klyce & Wilson,* 1989). The computer assisted photokeratoscopy, despite using statistical procedures, has its own disadvantages arising from the errors in accurate enlargement of the original image inherent with dimensionally unstable photographic paper and the manual digitisation process itself (*Klyce & Wilson,*1989). The manual digitisation even with a carefully trained operator introduces errors caused by static electricity and by involuntary hand tremor. It is also time consuming as each photograph requires about 10 min of encoding by a trained technician (*Klyce,* 1984).

1.3.4.4. *Accuracy of photokeratoscopy*

Using the visual inspection technique, clinically significant amounts of corneal cylinder up to 3 D may not be detected (*Wilson & Klyce,* 1991a). Quantitative analysis has an accuracy limited to 1 to 2 D. There are studies suggesting that clinically significant alterations of corneal contour like early keratoconus (*Maguire & Bourne,* 1989a), or contact lens-induced corneal warpage (*Wilson et al,* 1990a), are commonly not detectable with photokeratoscopy. On the other hand, in cases where more striking corneal changes occur, photokeratoscopy has been useful. These cases include post-radial keratotomy corneas (*Rowsey et al,* 1988), adjustment of a single running suture in penetrating keratoplasty (*McNeill & Wessels,* 1989), selective suture removal after penetrating keratoplasty (*Harris et al,* 1989).

1.3.5. Computer assisted videokeratography (CAVK)

The introduction of computers came as a logical advance from the basic principles of keratometry and photokeratoscopy developed over the preceding years. Computer Assisted Videokeratography (CAVK) precisely analyses the radius of curvature and corresponding refractive power (D) at thousands of locations across the corneal surface.

The introduction of the Corneal Modelling System (CMS) (*Gormley et al,* 1988; *Mammone et al,* 1990) manufactured by Computed Anatomy, NY, was the breakthrough in the era of computerised corneal topographic analysis and the first model of a series of videokeratoscopes to follow. The CMS could receive topographic and pachymetric information (with a dual-beam scanning laser slit lamp), measuring both refractive power and pachymetry at any point. At about the same time (*Koch et al,* 1989; *El Hage,* 1989), two more commercially available devices (EyeSys and EH-270) were introduced. Today, there are at least nine available CAVK systems [table 1.2].

1.3.5.1. *Theory and principles of operation of CAVK systems*

Corneal topography measurements can be achieved in a different of ways but all CAVK systems have some common principles of operation. These are: 1) some

TABLE 1.2 : Currently commercially available computer-assisted videokeratographers

CAVK model	Manufacturer	Data collection method	Corneal coverage	No of data points	Source of central cornea data	Dioptric range (D)	Average working distance
TMS-1	Tomey technologies	Placido cone; 25 or 32 rings	0.4 - 11 mm	7,186 (25 ring) 8,704 (32 ring)	Measured	9-109	40 mm
EyeSys 2000	EyeSys technologies	Placido cone; 9 rings	0.5-10 mm	6,480	Interpolation	9-99	90 mm
C-Scan	Technomed	Colour coded Placido disc; 15 rings	0.2~10.8 mm	18,800	Measured	10-100	
CM-1000	Topcon	Placido disc;15 rings	1-10 mm	10,440 sampled 5,400 analyzed	Interpolation	10-1000	
EyeMap (EH 290)	Alcon	Placido disc;23 rings non linearly spaced	0.46-10 mm	8,280	Measured	18-95	117 mm
Keratron	Optikon 2000	Placido cone;26 or 32 rings	0.33-10.7 mm	6,656 or 8,192		10-100	
MasterVue	ORC	Placido cone;22 rings, dual camera	0.3-8.3 mm	8,640	Measured	9-109	105 mm
CTS	PAR Vision Systems Corp	Rasterstereography (projected grid)	Entire	1,800	Measured	Unlimited	
Orbscan	Orbtek	Projected slits	Entire	~ 9,000	Measured	10-99	

form of *light (target)* is projected onto the cornea. Some methods are based on reflections, others on stereophotography or holographic interference 2) the modification of this light by the cornea is captured by a *video camera.* 3) the information (either a virtual or real image) is analysed by *computer software* (algorithms) that allow a reconstruction of the corneal surface. 4) the *data* are *displayed* in a variety of formats.

1.3.5.2. *Imaging the corneal surface - The target*

The most commonly used target is geometrically similar to the Placido disc or cone with concentric circles of light or mires. This form of target has the advantage of having the same symmetry as the cornea, so data points can be obtained along as many corneal meridians as desired (*Klyce & Wilson,* 1989). The mire pattern and number differ between instruments; some use a back lit conical dish (EyeSys), others a cylindrical light cone (TMS, MasterVue) and one instrument (C-Scan, Technomed) uses colour-coded ellipsoid Placido rings that can be distinguished and identified even when merging or broken on an irregular cornea. The area of corneal coverage with the Placido targets varies between instruments from a minimum of 0.2 mm to a maximum of about 11 mm [table 1.2]. There is one commercially available instrument which uses a projected grid as a target and utilises the raster-stereography technique (CTS, PAR Vision Systems Corp.) (*Belin et al,* 1992). The grid pattern covers the entire cornea and has also the advantage of being the only system currently that can be mounted directly on a surgical microscope (*Belin,* 1993). Another system (Orbscan, Orbtek) uses projected slits as a target.

The working distance is different between instruments and varies considerably from 10 mm for the TMS-1, to 144 mm for the EyeMap system. Generally to achieve the same corneal coverage, a longer working distance design requires a larger diameter Placido disc.

The focusing methodology also varies between different devices, and some of them (EyeSys 2000, Keratron, C-Scan, MasterVue, CM-1000) use hardware or software autofocus systems. Others such as the TMS-1 rely upon superimposing two laser beams on the centre of the cornea.

1.3.5.3. *Acquisition of the corneal image - the videocamera*

A real time video camera (equivalent to the photocamera in photokeratoscopy) captures the virtual image of the Placido reflections. Digital video cameras are used instead of the old style analog video cameras because the latter introduce errors due to inherently instability. Digital videocameras capture the images on a semiconductor circuit array and so dimensional stability is guaranteed by fixed optics and sensor by comparison to an electronically scanned electron beam (*Klyce & Wilson,* 1989). The videocameras used are Charge Coupled Devices (CCD). That means that they utilise a solid state sensor which translates light from a lens into electronic signals. CCD cameras used by all systems have a 512 x 512 pixel resolution, but this can be increased up to two or three times to subpixel accuracy by using edge-detection image processing algorithms (*Hachicha & Simon,* 1988).

1.3.5.4. *Image processing (analysis)*

The next step for the digitised image formed in the solid state videocamera sensor, is to be analysed by the computer. This procedure includes the following two steps: a) first *a reference point has to be established.* The computer locates automatically the centre of the smallest width ring. This is determined either by computational techniques to calculate either the centroid of the corneal surface area (*Klyce,* 1984), or its geometrically averaged centre (*Maguire et al,* 1987a). b) The estimated central position is used to convert the picture (each data point where a semimeridian intersects a mire), into *polar coordinates.* This has the effect of turning the nearly circular mires into nearly straight lines that are more easily identified by image analysis technology (*Klyce & Wilson,* 1989). In general the more points analysed on the corneal surface, the closer they are to each other and the higher the spatial resolution will be.

1.3.5.5. *Reconstruction of the corneal surface (reconstruction algorithms)*

After the transformation of the image to data recognisable by the computer, these must now be used in order to reconstruct the corneal profile and determine the optical power.

Generally speaking any instrument designed to determine the entire corneal contour, must either i) determine the radius at known points over the corneal surface, with these points having a known separation; then by interpolation the radii of intermediate points may be determined, or ii) determine the departure of the corneal curvature from a known mathematical model (*Stone,* 1962). However with the exception of the central zone, the corneal curvature departs from any known mathematical curve. Therefore although the second method should give a truer reproduction of the corneal form, so far the several approaches that have been reported for this purpose (*Doss et al,* 1981; *Klyce,* 1984; *Wang et al,* 1989) utilise the first method. For this purpose equations (reconstructive algorithms) are applied to the location of each point. The algorithms are mathematical formulas from which the curvature of the cornea is calculated. All of the proposed calculations rely upon various assumptions [table 1.3] but we do not know exactly which algorithms are used in each of the current commercially available CAVK units as these are considered proprietary by their manufacturers.

1.3.5.6. *Corneal presentation schemes*

The presentation of the videokeratographic data should have a meaningful appearance if it is to be easily understood by the eye surgeon. There are four basic methods of displaying corneal topographic information. 1) the videokeratography picture itself [figure 1.2], 2) dioptric power measurements on different radii on the corneal surface [figure 1.3A], 3) Three dimensional wire mesh representation of

TABLE 1.3 : Different corneal profile reconstruction algorithms and assumptions used

Algorithm	Doss et al, 1981 (1)	Klyce, 1984 (2)	Wang et al, 1989 (3)
Input data	Radius of individual rings along specified corneal radii	as in (1), but more meridional calculations made	as in (2)
Reconstruction of corneal profile and calculation of R	Semicordal lengths from image centre and multiple arc technique	multiple arc technique as in (1)	angle sustained by two adjacent points of the virtual image
Reference	a 7.8 mm radius of curvature	the average R calculated from the first keratoscopic corneal ring image	as in (2)
Optical power calculation	Ray tracing technique P = 1,000 / F.D	Arc analysis technique P = 0.3375 / R	as in (2)
ASSUMPTIONS			
1) The cornea has a continuous spherical regular surface	+	+	-
2) Curvature locally constant	+	+	+
3) effect of astigmatism is neglected	+	+	+
4) Normal cornea has R=7.8 mm	+	-	-
5) Surface plane is tangent to corneal surface	+	+	+
6) Reference point	corneal apex	centre of the first ring	centre of first ring
7) spherical approximations for calculation of power	+	+	+

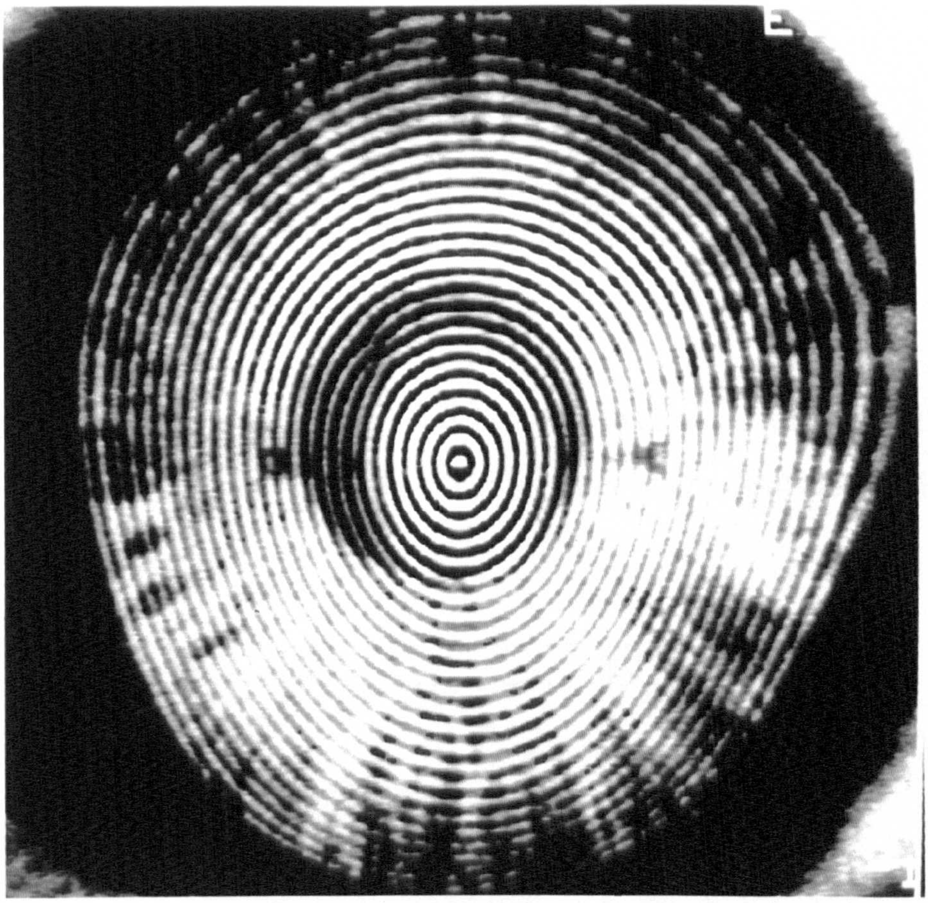


Figure 1.2 : Example of a videokeratography picture obtained with the TMS-1, in a patient with pellucid marginal corneal degeneration.

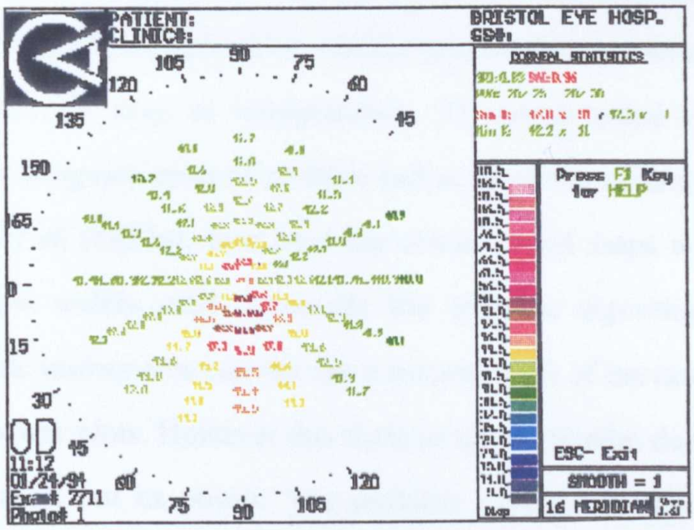


Figure 1.3A : Example of a numeric display map obtained with the TMS-1. This is a map of colour-coded numeric values (dioptres in this case) displayed along 16 meridians.

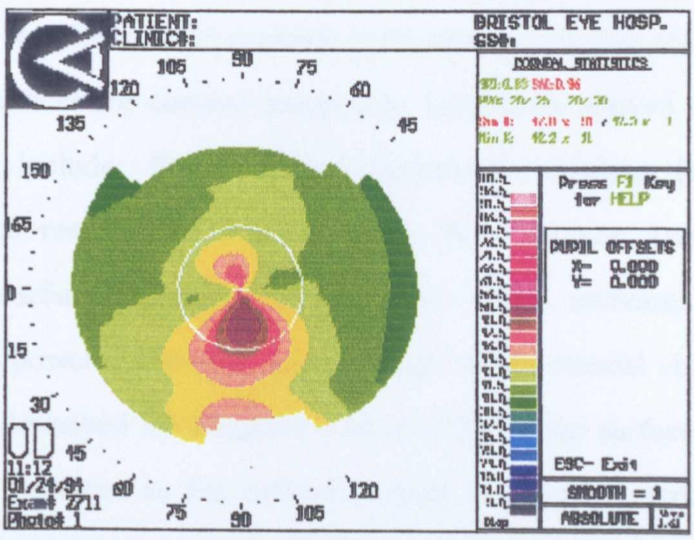


Figure 1.3B : Example of a colour-coded map (absolute scale) obtained with the TMS-1.

the corneal reconstruction was attempted first by *Itoi & Maruyama* (1978) from photokeratoscope data, and later by *Klyce* (1984), *Gormley et al.* (1988), and *Young & Siegel* (1993a,b). This kind of presentation however failed in practice to prove clinically easy in interpretation. 4) colour-coded maps using different colours to designate areas of uniform radius of curvature and power [figure 1.3B]. *Maguire et al.* (1987a), first used the colour coded maps with the LSUCTS and this is now widely used. Typically the software algorithms employed by the topographic instruments convert the measured radii of curvature into colour-coded dioptric power plots. However this form of representation does not show the shape of the cornea, but its power. The problem with that is that while clinicians are more familiar with refractive power than with contour maps, a misconception that the power plots themselves represent the actual corneal surface contour, may arise.

1.3.5.7. *Parametric quantitative descriptors of corneal topography - Corneal statistics*

The qualitative information that is provided by colour coded maps is sometimes not adequate for clinical and research applications. For this reason a number of quantitative indices for corneal topography have been derived and are currently used. These include: the simulated keratoscope reading (simk), an index mimicking the readings of a keratometer; the minimum keratoscope reading (mink); the surface asymmetry index (SAI) which increases with increasing asymmetry in power distribution and correlates with potential visual acuity (PVA) as originally described by *Dingeldein et al.* (1989); the surface regularity index (SRI) which increases as the central corneal irregularity increases and is also directly correlated to the patient's visual acuity (*Wilson & Klyce*, 1991b).

1.3.5.8. *Accuracy and precision of CAVK*

A significant amount of research has taken place regarding the accuracy and repeatability of CAVK devices on test surfaces, mainly calibrated test spheres and normal corneas. The results show an acceptable level of accuracy and reproducibility for different commercially available models of CAVK (*Koch et al,* 1989; *Hannush et al,* 1989 and 1990; *Wilson et al,* 1992a; *McCarey et al,* 1992; *Koch et al,* 1992; *Legeais et al,* 1993; *Maguire et al,* 1993). CAVK has been found to be more accurate (within 0.25 D) than keratometry and Corneascope (*Hannush et al,* 1989; *Wilson et al,* 1992a), but the accuracy was much reduced for very steep or flat corneas (*Hannush et al,* 1989; *Legeais et al,* 1993). On the other hand, the keratometer appears to be more reproducible than CAVK (*Hannush et al,* 1990; *Legeais et al,* 1993), or at least equally reproducible (*Hannush et al,* 1989). All three instruments (keratometer, photokeratoscope and CAVK) are based on some assumptions, a number of which they share.

1.3.5.9. *Limitations of CAVK*

There are some sources of inaccuracies in CAVKs that create some limitations on the use of these instruments. These inaccuracies may arise from the instrument itself, or from the algorithms used.

Inaccuracies from the instrument itself

1) CAVKs examine the air-tear film rather than the corneal surface itself (a limitation shared as well by keratometer and photokeratoscope). Irregularities of the tear film may cause incorrect measurements or missing data for computing, as it is the tear-film interface rather than the anterior corneal surface that is reconstructed.

2) *Focusing* : an error of just 1mm has been demonstrated to create topographic data which is inaccurate by 1.5 D (*Mandell,* 1992). Such errors are likely to be dependent on the working distance of the device. Instruments with a short working distance are more likely to produce higher defocusing errors.

3) *Misalignment* : In order for the CAVK to fulfil many of the assumptions made by the reconstructive algorithms, the cornea must be correctly positioned (*Wang et al,* 1991). Small errors in alignment can result in an irregular or asymmetric

topographic reconstruction. In one commercially available instrument (EyeSys) poor fixation has been shown to produce a pattern of pseudokeratoconus; the increase in relative steepness was statistically significant at 5 degrees of deviation (*Hubbe & Foulks,* 1994).

4) Interpretation of the data provided by the CAVK is quite subjective.

Inaccuracies from the algorithms

1) there is no known mathematical formula which describes exactly the shape of the normal cornea; therefore the algorithm whatever it is gives an approximation of the corneal shape. This tends to be more accurate towards the centre where the cornea approximates a sphere. *Roberts* (1994a), has demonstrated that one CAVK system (EyeSys) does not accurately measure meridional curvature in radially aspherical surfaces. The maximum error was greater than 3 D at a radius of 4 mm for a surface with an apical radius of curvature of 7.5 mm and an eccentricity of 0.5. The sensitivity of TMS has also been found to be reduced on peripheral cornea, even when measuring calibrated spheres or normal corneas (*Hannush et al,* 1989 and 1990).

2) in order that each point on the mire reflection corresponds to a unique position for the cornea, a number of assumptions should be made (*Wang et al,* 1989 and 1991). These assumptions may not be valid.

3) The direct correlation between corneal power curvature and power (with which clinicians are familiar) is not valid in the peripheral regions of the cornea. CAVK devices measure curvature and not corneal power; the two are interchangeable only in the central corneal region (*Roberts,* 1994b). In the corneal periphery, the spherical assumption introduces errors of 2 to 3 D (*Mandell,* 1992; *Klein,* 1992).

4) CAVK are much less accurate in measuring very steep and very flat corneas (*Hannush et al,* 1989; *Legeais et al,* 1993).

1.3.5.10. <u>*Current clinical and research applications of CAVK*</u>

Computer-assisted videokeratography has a broad range of applications that the clinician could use in order to better understand the corneal contour and improve the management of patients. An account of the most common current applications of CAVK is given below.

Topography of normal corneas : Clinical studies have attempted to evaluate the topographic appearance of normal corneas. In the most extensive study to date with the aid of CAVK, *Bogan et al.* (1990) examined 399 normal eyes with the Corneal Modelling System (CMS, Computed Anatomy Inc, NY). The authors found that the central zones of uniform curvature were seen as round in 23%, oval in 21%, symmetric bow tie in 32% and irregular in 7%. Each of these patterns was observed in corneas without keratometric or refractive astigmatism. It is therefore important that a variability in pattern is recognised among normal corneas, covering a whole spectrum from round to irregular.

Diagnosis of keratoconus and other ectatic diseases : CAVK is a sensitive method for early diagnosis of keratoconus when clinical evidence is absent (*Maguire & Bourne,* 1989a). The old hypothesis of keratoconus being an autosomal dominant disorder (*Amsler,* 1938) was supported after a study with CAVK showed that family members had topographic patterns similar but less severe than those in patients with keratoconus (*Rabinowitz et al,* 1990). The topography of established keratoconus has been studied with CAVK in a few series (*Wilson et al,* 1991a; *O'Brart et al,* 1994; *Bryce et al,* 1995). Proposed topographic subtypes include: oval with cone usually inferiorly, globus variation, nipple variation, and astigmatic subtype. Recently an automated keratoconus screening based on quantitative topographic data, has been proposed (*Maeda et al,* 1994). The validity of this system in everyday clinical practice remains to be seen. CAVK has also been used to assess pellucid marginal corneal degeneration (*Maguire et al,* 1987b), pellucid marginal degeneration and keratoglobus (*Karabatsas & Cook,* 1996), posterior keratoconus (*Mannis et al,* 1992) and Terrien's marginal degeneration (*Wilson et al,* 1990b).

Contact lens fitting : Contact lens fitting of complex cases using topographic information from CAVK rather than from keratometry alone, may give quicker and more accurate initial fits (*Rabinowitz et al,* 1991; *Wasserman et al,* 1992; *McDonnell et al,* 1992; *Lopatynsky et al,* 1993).

Contact lens induced warpage : Corneal lens induced warpage was studied with the aid of CAVK by *Wilson et al.* (1990a). This study showed that the time taken for the cornea to return to a stable shape can be as long as 5 months in some cases and that generally the cornea was flattened beneath the resting position of a rigid contact lens with relative steepening 180^{o} away.

Analysis of corneal shape after radial keratotomy (RK) : After radial keratotomy, zones of central corneal flattening are typically centred around the corneal apex (*McDonnell et al,* 1988; *Bogan et al,* 1991). It has also been demonstrated that a significant factor in the variability of refraction in post radial keratotomy patients is due to a multifocal effect from the cornea which also explains the monocular ghost images experienced by some of these patients (*McDonnell et al,* 1988; *Maguire & Bourne,* 1989c). In another study, the changes in corneal curvature after RK, were attributed to changes in corneal thickness (*Kwitko et al,* 1992).

Post laser treatment for myopia : CAVK has also been used in studying central photorefractive keratectomy (PRK) for myopia with the excimer laser (*Maloney,* 1990; *McDonald et al,* 1990; *Cantera et al,* 1993; *Klyce & Smolek,* 1993; *Lin,* 1994). The well recognised regression effect in an advanced myope after PRK has been shown with CAVK (*McDonald et al,* 1990). Quantification of excimer laser treatment, including its relationship to the pupil, can also be displayed with CAVK (*Wilson et al,* 1991b; *Cavanaugh et al,* 1993).

Epikeratophakia : Corneal topographic analysis demonstrated corneal surface steepening in epikeratophakia for aphakia (*Maguire,* 1990), and flattening in epikeratophakia for myopia and keratoconus (*Maguire et al,* 1987c).

Following PKP : CAVK has been used as a guide in selective suture removal after PKP, to identify the steepest corneal semimeridian (*Strelow et al,* 1991).

Topographic changes occurring following removal of 10-0 running suture after PKP have been looked at by *Lin et al.* (1990a). The healing process of the cornea after PKP has been studied by *Khong et al.* (1993) with the aid of CAVK.

Surgical correction of astigmatism : The role of CAVK in planning surgical treatment for naturally occurring or postoperative astigmatism has been looked at by *Frangieh et al.* (1991).

The use of CAVK in the assessment and management of astigmatism is the major issue of this thesis and examined separately in the following chapters.

1.3.6. Rasterstereography

In rasterstereography a calibrated grid of horizontal and vertical parallel lines is projected either on the tear film of a fluorescein-stained cornea or on a drape covering the cornea. The pattern of this grid makes it possible to collect a mesh of data points equally spaced on the corneal surface, in contrast to the circular keratoscope mires. The *real* image of this target is captured from a fixed angle and then automatically digitised by a camera in a similar way as with the CAVK devices. Each row of the image is then scanned from one side to the other in order to identify the position of each image line within the captured image (*Warnicki et al,* 1988). The method calculates elevation of the surface (*Arffa et al,* 1989) directly, rather than corneal curvature. It has the advantages of not requiring a smooth reflective surface or precise spatial alignment for accurate imaging (*Belin & Zloty,* 1993) and also of covering the whole of the corneal surface. PAR Technology (New Hartford, NY) has commercially introduced such a system (*Belin et al,* 1992; table 1.2). The method can also be used as an intraoperative technique (*Thall & Lange,* 1993; *Belin,* 1993). Rasterstereography although having theoretical advantages over Placido based systems in measuring aspherical surfaces, lacks in sensitivity as this is limited by abnormalities in the tear film or diffusion of fluorescein in the stroma. For a precision of 0.25 D to be achieved, elevation must be measured with a precision of 2.5 μm; however the fluorescein-stained tear film or the conforming drape are several times thicker than that (*Missotten,* 1994).

1.3.7. Interference fringe techniques

Two wave fronts of light creating interference fringes on the corneal surface can produce extremely accurate measurements, less than the wavelength of the light used. There are two methods of measuring corneal contour based on this principle, but they have not yet found clinical applications, at present being used mainly as research tools.

Moire fringe analysis : Moire fringes are a more complex form of surface imaging than rasterstereography, requiring two grid patterns projected on the cornea. In the areas where the rulings overlap, an interference fringe pattern forms (*Mandell,* 1966; *Kawara,* 1979). The moire fringe pattern can be photographed and analysed in a similar manner to rasterstereography.

Laser holographic interferometry: This technique also utilises wave interference to measure corneal topography. Holography works by revealing the strain over the ocular surface caused by small stresses such as changes in intraocular pressure from the ocular pulse (*Holladay & Waring,* 1992). Its major advantage is the ultrahigh precision of the measurements (less than a wavelength of the probing wave). Although not yet clinically available, the technique has been used to measure in vitro the flattening of the cornea with the intrastromal ring (*Burris et al,* 1993).

1.3.8. Corneal pachymetric topography

A new technology that produces pachymetric maps of the corneal epithelium and anterior corneal tissue was described and termed by *Reinstein et al.* (1994). The system uses high frequency ultrasound scanning enhanced by digital signal processing. Measurements are made with a precision of 2 μm SD. Pachymetric maps are constructed by plotting local thickness represented by a colour scale.

1.4. ASTIGMATISM - BASIC CONCEPTS

The optical condition in which the refractive power of the eye varies in different meridians is called astigmatism. This means that the incident light rays are not equally refracted in all meridians and the image is formed as a Sturm's conoid (*Elkington & Frank,* 1991) failing to come to a point focus. The astigmatic eye produces instead two separate line foci and the difference in power in the principal meridians represents the amount of astigmatism. The term derives from the Greek [α:(privative) + στιγμα (stigma = point)], referring to the inability of the eye to produce a point image from a point light source.

1.4.1. History

As early as 1670 Isaac Barrow and Isaac Newton at Cambridge, became aware of the production of astigmatism by oblique pencils of rays on a spherical lens (*Levene,* 1965). Nevertheless, astigmatism as a refractive error only began to be understood in the early 19th century, at the same time as the comprehensive physical theories were available. *Thomas Young,* in the early 1800s discovered astigmatism by noting the difference in focusing horizontal and vertical lines in his own eyes. He also demonstrated that the cause of that was a tilting of the crystalline lens of his eye. The correction of astigmatism using cylindrical lenses was first described by the astronomist *George Airy* who independently discovered astigmatism in his own eye about 25 years after Young (1827). The term "astigmatism" was suggested to Airy, by Dr. William Whewell, Master of Trinity College. However, it was only in 1850, that *George Gabriel Stokes,* a Cambridge physicist, introduced cylindrical lenses to correct astigmatism (*Levene,* 1965).

1.4.2. Classification of astigmatism

Astigmatism can be caused by the cornea, the lens, or both. Astigmatism of corneal origin called *corneal astigmatism,* is by far the most important and common cause. The cornea becomes astigmatic whenever it assumes a toroidal shape, which means that one maximum and one minimum radii of curvature, called principal meridians can be identified. In the case of lens origin, the astigmatism is called *lenticular.* This kind of astigmatism usually accounts for small degrees of refractive error, except when the lens is markedly displaced as it may occur in certain conditions such as Marfan's syndrome.

Astigmatism is said to be *regular* when the principal meridians are approximately 90^o apart and the radius of curvature changes gradually from one meridian to the other. In the case of *irregular* astigmatism the two principal meridians are separated by an angle other than 90^o, or two principal meridians may not even be identified when the contour of the cornea is very distorted. While regular astigmatism in most cases can be satisfactorily corrected with cylindrical lenses, irregular astigmatism cannot; rigid contact lenses can be used instead, or keratorefractive surgery if it is significant. Irregular astigmatism also induces optical aberrations.

In the literature the terms "with-the-rule" and "against-the-rule" astigmatism are also used. *With-the-rule astigmatism* is when the greatest refractive power of the cornea (steepest meridian) is near vertical in orientation or close to 90^o. This condition is corrected by placing a plus cylinder in the vertical meridian (or a minus cylinder in the horizontal meridian). *Against-the-rule astigmatism* means that the greatest refractive power is close to the horizontal 180^o. Respectively if the principal meridian of astigmatism is more than 20^o away from the vertical or horizontal axis, the astigmatism is called *oblique.*

With the introduction of CAVK the concept of semimeridians instead of meridians for description of the corneal topography has been introduced. This leads to a new classification of corneal astigmatism (*vide infra*).

On a different classification, astigmatism can be divided into *naturally occurring* and *iatrogenic or surgically induced astigmatism* depending on the causative factor.

1.4.3. Naturally occurring astigmatism

Almost all individuals with naturally occurring astigmatism have regular astigmatism. A large amount of evidence suggests that astigmatism is hereditary. *Solsona* (1975), estimated that 65.5% of astigmatism present in patients is congenital, bilateral and symmetrical and that the 'sum' or fusion of two symmetrical monocular astigmatisms produces a binocular image almost free of astigmatism. The incidence of with the rule astigmatism tends to increase during the early years of life but remains relatively constant during the school years. During early adult life astigmatism changes very little, but later there is a strong tendency to change to against-the-rule astigmatism (*Grosvenor,* 1978). There are different theories on the development of physiological astigmatism. These include the theory of contraction of extraocular muscles, the lid pressure theory (*Gullstrand,* 1924), or a result of growth (*Weale,* 1983). Nevertheless *Long* (1982), has shown that no biological explanation is necessary, but regular astigmatism is a consequence of local toricity of the ocular surface.

1.4.4. Surgically induced (iatrogenic) astigmatism

This kind of astigmatism results primarily from deformation of the cornea by surgery. It can be induced by many surgical procedures including retinal surgery, cataract surgery, corneal graft surgery and corneal surgery in general including refractive surgery (*Swinger,* 1987). For the purpose of this thesis only the postoperative astigmatism following penetrating keratoplasty will be discussed and analysed further, as it is the main parameter of this study.

1.4.5. Measurement of astigmatism

The classic methods of measuring astigmatism are refraction and keratometry. With the recent developments however in photo and videokeratoscopy, alternative ways of looking at the astigmatism have gained interest.

1.4.5.1. *Refraction*

Clinical refraction measures the spherocylindrical lens required to correct the refractive error of the whole optical system. While this is essential when prescribing a spectacle correction, it is not that accurate in assessing corneal astigmatism as it takes into account the refractive changes of the lens. It is also a subjective technique when we refer to the manifest refraction, but may also be obtained objectively when retinoscopy or autorefractometry are employed. Refraction can be performed with or without cycloplegia. Sometimes the full amount of cylinder measured by refraction may not be accepted by the patient.

1.4.5.2. *Keratometry*

This method of acquisition of information on the shape of the cornea has been discussed in detail in chapter 1.3.2. It is clear that keratometry and refraction measure different astigmatisms; keratometry measures exclusively corneal astigmatism whereas refraction measures the total astigmatism of the eye. The magnitude of corneal astigmatism is the difference in diopters between the refractive powers of the principal meridians. Early in 1890, Javal studied the relationship between the two ways of measurement, and proposed his famous empirical rule for predicting the subjective astigmatism based on the keratometer finding. $At = k + p\ (Ac)$ where At = total astigmatism of the eye; Ac = corneal astigmatism; $k = 0.50$ approximately; and $p = 1.25$ approximately.

1.4.5.3. *Keratoscopy and Photokeratoscopy*

These methods have been discussed in detail in chapters 1.3.3 and 1.3.4.

1.4.5.4. *Computer assisted Videokeratography (CAVK)*

With CAVK, astigmatism is typically shown by the presence of a band of relative corneal steepening ("hot colours" in topographic maps), that may or may not be narrowed centrally so as to have a bow-tie configuration. Although this steepening is frequently symmetrically distributed around the corneal apex, there may be a steepening primarily in one semimeridian with very little steepening in the semimeridian 180° away (*McDonnell,* 1991).

Our understanding of astigmatism has been improved by CAVK. Based on videokeratographic pictures we can now divide regular and irregular astigmatism into *symmetric* and *asymmetric*, depending on the difference of dioptric power between semimeridians and the configuration of the topographic pattern.

Regular astigmatism is demonstrated by the classical bow-tie pattern on corneal topography, with an angle between the steep meridian and flat meridian of 90°. Symmetrical astigmatism occurs when there is equal dioptric power or steepness on either side of the optic axis along the primary steep or flat meridian. Additionally, the steepest and flattest axes of the cornea may not always be orthogonal (*Bogan et al,* 1990) as expected in spherocylindrical optics. So, the concept of "irregular astigmatism" was understood better with CAVK. This kind of astigmatism is particularly common after surgery and keratoplasty.

1.4.5.5. *Calculation of surgically induced astigmatism*

In order to determine the change in astigmatism induced by a surgical procedure, both the preoperative and postoperative measurements are necessary. Several methods for this are employed. The simple subtraction method of calculating cylinder difference without regard to the axis is the simplest way. Although clinically useful, this method is not adequate for quantitative change in astigmatism, as it takes in account only the magnitude of the cylinder but not the axis. In order to calculate the actual change in corneal shape, other methods can be used. These are called 'vector-analysis methods'. They all treat the component power of astigmatism as vector in a vector diagram directed at angles twice the actual angle of orientation before the eye (*Naylor,* 1968; *Jaffe & Clayman,* 1975; *Cravy,* 1979; *Naeser,* 1990; *Holladay et al,* 1992; *Kaye et al,* 1992; *Alpins,* 1993).

These methods are useful in determining the amount of surgically induced astigmatism, which can be done by trigonometric calculations [appendix V] or with simple calculator programs.

1.5. POSTKERATOPLASTY ASTIGMATISM

1.5.1. Penetrating keratoplasty

The major reason for doing a penetrating keratoplasty (PKP) is to replace the central portion of a scarred or distorted cornea by a clear button of regular donor tissue. Corneal transplantation remains the most frequently reported organ transplant in the UK (*UKTSSA*, 1994) and in Australia (*Coster*, 1991).

1.5.1.1. *History*

Corneal xenografts (from chickens to rabbits) were first attempted by *Reisinger* (1824), a German surgeon who also first used the term "keratoplasty". Later, *Bigger* (1837), performed the first successful animal allograft by taking tissue from a wounded, dying gazelle and transplanting it to a blind gazelle. *Kissem* (1844), performed the first -although failed- human xenograft using a pig cornea as donor. The first technically successful human corneal allograft was reported by *Sellerbeck* (1878). This graft however clouded after 20 days and credit for the first success is more often given to *Zirm* (1906), an Austrian-born surgeon working in the small town of Olutz in Czechoslovakia, who performed a graft that remained clear for over one year. These early grafts used fresh donors tissue. Transplantation of cadaver tissue was introduced by *Filatov* in 1931, opening a new era in corneal transplantation. By 1955, 8400 corneal grafts had been performed in the Soviet Union (*Filatov*, 1957).

1.5.1.2. *Present indications for keratoplasty*

There are four indications for penetrating keratoplasty : 1) visual, in order to improve sight impaired by disease, 2) therapeutic, in order to remove infected, damaged or painful tissue, 3) tectonic, to re-establish the integrity of the eye following perforation or thinning of the cornea, 4) cosmetic, to improve appearance following scarring of the cornea.

The majority of corneal grafts are performed for visual indications. In the United States 40,000 corneal grafts are performed annually (*Nenno & Abel,* 1991). Table 1.4 summarises the indications and incidence of diagnoses for penetrating keratoplasty as shown in recently published large series.

1.5.1.3. *Penetrating keratoplasty technique*

A detailed discussion of surgical technique in PKP is described in the materials and methods section of chapter 4. The basic steps of the technique are: stabilisation of the eye with a support ring, donor trephination, recipient's cornea trephination, and suturing of the donor tissue in place.

1.5.1.4. *Graft survival*

Advances in preoperative assessment, surgical techniques and instrumentation, donor material, immunossupressive medications and postoperative care, have resulted in a higher percentage of clear corneal grafts. Rejection is the main cause of graft failure (*Bradley et al,* 1993; *Williams et al,* 1993). Today, a clear corneal graft is expected in about 90% of cases at one year following PKP (*Australian Corneal Graft Registry,* 1989; *Williams et al,* 1993; *Vail et al,* 1994). The overall survival declines slightly with time, to about 72% of cases at five years follow up (*Williams et al,* 1993). The survival rate may be better for keratoconus cases, reaching a 97% five year survival (*Kirkness et al,* 1990). For high risk cases such as regrafts and deep vascularization the risk of failure almost doubles (*Bradley et al,* 1993); for therapeutic PKP, the survival rate may be as low as 54% (*Killingsworth et al,* 1993). Table 1.5 summarises corneal graft survival rates.

TABLE 1.4 : Indications for penetrating keratoplasty

Study	Period of study	No of patients	Country of study	Keratoconus	Fuch's dystrophy	PBK	ABK	Regraft	HSK	Infection	Trauma	other
Australian Corneal Graft Registry, 1989	1985-1989	1485	Australia	475 (33%)	64 (4.3%)	193 (13%)	137 (9.2%)	194 (13%)	43 (3%)	14 (1%)		333 (22.4%)
Mamalis et al, 1991	1981-1988	740	USA	169 (22.8%)	43 (5.8%)	161 (21.8%)	47 (6.4%)	98 (13.2%)	25 (3.4 %)		6 (0.8 %)	191 (25.8%)
Lindquist et al, 1991	1980-1988	1594	USA	380 (23.8%)	198 (12.4%)	273 (17.1%)	73 (4.6%)	129 (8.1%)	98 (6.1%)	55 (3.5%)	23 (1.4%)	365 (22.9%)
Vail et al, 1993	1987-1991	4560 *	UK & Republic of Ireland	634 (19.9%)	363 (11.4%)	481 (15.1%)	221 (6.9%)	576 (18%)	338 (10.6%)		102 (3.2%)	469 (14.7%)
Sharif & Casey,1993	1971-1990	3555	UK	597 (16.8%)	140 (3.9%)	72 (2 %)	210 (5.9%)	1452 (40.8%)	417 (11.7%)	6 (0.1 %)	105 (2.9%)	534 (15%)
Williams et al, 1993	1985-1991	3608 §	Australia	1071 (31%)	170 (4.7%)	577 (16%)	165 (4.6%)	478 (14%)	104 (3%)	18 (0.5%)		877 (24.3%)

PBK = Pseudophakic bullous keratopathy, ABK = Aphakic bullous keratopathy, HSK = Herpes Simplex Keratitis

* 3184 cases with recorded diagnosis
§ includes 148 lamellar grafts

TABLE 1.5 : Corneal graft survival

Study	No of patients	Patients Diagnosis	SURVIVAL RATE 1 year	2 years	3 years	4 years	5 years	Variable FU
Cherry et al, 1979	351	Variable	72 %					
Ficker et al, 1989	127	HSK						70% *
Australian Corneal Graft Registry, 1989	1064	Variable	92 %	90 %	86 %	86 %		
	383	Keratoconus				98 %		
	70	Dystrophies				88 %		
	137	PBK				82 %		
Kirkness et al,1990		Keratoconus					97 %	
Australian Corneal Graft Registry, 1993	2248	Variable	90.8 %	84 %	80 %	74 %	72 %	
Killingsworth et al, 1993	80	Therapeutic PKP						54% ⊗

* longterm (over 20 years FU) for first graft in quiet eyes
⊗ FU variable (1 month to 9 years)

1.5.2. Incidence of postkeratoplasty astigmatism

High postoperative astigmatism is a frequent problem following PKP. The incidence of this astigmatism had been estimated approximately 10% for 5-6 D of keratometric astigmatism (*Troutman & Swinger,* 1980). This appears to be an underestimation, as later studies have reported 25% of PKP with more than 4 D of astigmatism (*Binder,* 1988), 32% with more than 5 D (*Insler et al,* 1987). In the Australian Corneal Graft Registry (*Williams et al,* 1993), 19% of the eyes (about 1 in 5 grafts) demonstrated keratometric astigmatism equal or more than 5 D, whereas 34% of the eyes showed astigmatism less than 5 D (the rest of the eyes had either unreliable readings or not recorded astigmatism).

In keratoconic eyes the percentage of eyes with more than 4 D of astigmatism may be as high as 43% (*Troutman & Gaster,* 1980). There are great difficulties in comparing astigmatism found in previous studies due to the great variations in numbers, diagnoses, surgical techniques, method of measuring astigmatism and follow up. Mean astigmatism after PKP varies considerably in literature, averaging 4-6 D in most studies, although in some instances it has been as high as 8 D (*Jensen & Maumenee,* 1974; *Foulks et al,* 1979; *Perlman,* 1981; *Perl et al,* 1981; *Stainer et al,* 1982; *Bourne et al,* 1982; *Heidemann et al,* 1985; *Kirkness et al,* 1990; *Williams et al,* 1993), and is higher after PKP for keratoconus (*Wilson & Bourne,* 1989; *Kirkness et al,* 1991).

1.5.3. *Causes and pathophysiology of postkeratoplasty astigmatism*

A number of factors are believed to introduce excessive postkeratoplasty astigmatism. These can be seen in table 1.6 and discussed below.

TABLE 1.6 : Factors associated with postkeratoplasty astigmatism

Presurgical factors	Surgical factors	Postsurgical factors
Donor astigmatism/scars	Use of scleral ring	Wound healing
Host pathology	Trephine tilt	Timing of suture removal
Host astigmatism	Eccentric trephination	
	Donor preparation	
	Donor/host disparity	
	Use of IOL	
	Intraop keratometry	
	Suturing technique	

Original host and donor pathology

Grafting of keratoconic tissue with progressive stromal distortion has been considered as a probable explanation for decreased vision many years after surgery (*Rubinfeld et al,* 1990). The effect of recipient's pathology in the astigmatic outcome has been studied in few prospective studies. *Perlman* (1981) found higher astigmatism in aphakic patients, in contrast to what was observed in other studies (*Jensen & Maumenee,* 1974). No significantly different astigmatism between various diagnoses was observed in other studies (*Cherry et al,* 1979a). High pre-existing astigmatism in a laboratory study (*van Rij & Waring,* 1988) did not seem to produce irregular trephine opening.

Placement of the scleral fixation ring

Intraoperative placement of a scleral ring, particularly in aphakic patients, prevents the eye from collapsing and allows fixation of the globe and better reconstruction of the anterior segment. It has been postulated that the use of scleral fixation ring *per se* can introduce astigmatism by suturing it to the sclera (*Olson*, 1981). *Villacriz & Smith* (1986) were able to induce significant degrees of corneal astigmatism on human eye bank eyes, by varying suture placement and tension of Flieringa rings.

Host preparation (trephine tilt / excision of recipient button)

There are several ways of performing trephination of the host cornea during a PKP operation. Many corneal surgeons believe that the major cause for astigmatism induced by keratoplasty is an asymmetric trephination of donor and recipient corneas (*Olson*, 1980 and 1983; *Laroche*, 1987; *Kaufman*, 1989). Some surgeons use a free-hand technique followed by excision with scissors, where others use trephines which operate by suction or friction (*Duffin et al*, 1984; *Insler et al*, 1987) or are motor driven (*Pouliquen et al*, 1985; *van Rij & Waring*, 1988). There is evidence that suction trephines produce more uniform opening, but also cause undercutting (*van Rij & Waring*, 1988) and posterior bevel (*Duffin et al*, 1984).

The recent introduction of laser as a non-touch trephine has improved the configuration of the recipient and donor cut (*Serdarevic et al*, 1988; *Lang et al*, 1989; *Husinsky et al*, 1991). In a clinical study, astigmatism following PKP with 193 nm Excimer laser trephination ranged between 3.9 D to 4.6 D (*Naumann et al*, 1993).

Trephine tilt is thought to contribute to an oval wound and to wound disparity. *Troutman* (1979) estimated that a 0.1 mm of wound disparity translates into more than 1 D of astigmatism. *Olson* (1980), in a mathematical model calculated that for each 0.1 mm of wound disparity approximately 0.4 D of astigmatism is introduced. The theoretical effect of trephine tilt on postkeratoplasty astigmatism was also studied by *Krumeich et al* (1988); by mathematical analysis it was calculated that a trephine tilt as slight as 10^{o} on either the donor or the recipient with an 8-mm trephine can produce 5.8 D of astigmatism. Both the previously mentioned studies came to the same conclusion, that the smaller the trephine the larger the distortion. *Cohen et al.* (1986), using photogrametric analysis of endothelial button edges in eye bank eyes, observed that even when no attempt is made to tilt a hand-held trephine, oval and irregular wounds may result, and furthermore the ovality or asymmetry is not correlated with the angle of tilt. These findings differ from those of *Olson* (1980 and 1981) and *Krumeich et al.* (1988) probably because of the different methods of study used.

An oval graft in a round recipient bed, or a round graft in an oval recipient opening will induce astigmatism with the flatter meridian at the longer axis (*Troutman,* 1979; *Perlman,* 1981). By suturing a round donor button into an oval host bed in a rabbit model, *Villacriz et al.* (1987) found that increasing ovality of the recipient bed correlates with an increase in postoperative astigmatism.

Donor preparation (punch)

Anterior or posterior cutting of the donor button makes a difference in the final astigmatism (*Troutman,* 1979). Most corneal surgeons today follow the modified Amsler technique where the donor button is cut from the endothelial surface of a previously prepared corneoscleral disc from the donor globe, but this provides a graft anterior diameter 0.2 mm smaller than that of the host (*Troutman,* 1979; *Olson,* 1979).

Donor / host size mismatch

There is no general agreement between corneal surgeons on the use of same size or oversized donor buttons in PKP. The use of oversized corneal grafts was introduced to decrease postoperative hyperopia in aphakic patients and for the reduction of elevated intraocular pressure (IOP) in aphakic grafts (*Olson,* 1983). On the other hand, using a same size host-donor trephine carries the advantage of reducing the degree of post-PKP myopia in keratoconic patients (*Wilson & Bourne,* 1989) or infants (*Gloor et al,* 1992). In order to reduce postoperative myopia in keratoconic patients, grafts 0.25 mm smaller than the opening have been used; they have been reported to induce less astigmatism -but not statistically significant- than grafts larger than the opening (*Girard et al,* 1988 and 1992).

No significant difference in astigmatism between oversized and same size grafts was found in retrospective studies (*Foulks et al,* 1979; *Bourne et al,* 1982), and this was confirmed in a prospective randomised study (*Heidemann et al,* 1985). In the Corneal Transplant Follow-up Study (CTFS), preliminary analysis of factors influencing astigmatism, has found that astigmatism was worse with large donor-recipient trephine size differences (>0.25 mm) (*Bradley et al,* 1993). Table 1.7 summarises astigmatic results related to graft disparity, from different studies.

TABLE 1.7 : Postkeratoplasty astigmatism related to graft disparity [sutures are in place in some series] (table modified from *Binder,* 1985a and *Krumeich et al,* 1988)

Author	No of eyes	astigmatism§	donor/ host	Multiple surgeons
Boruchoff et al, 1975	42	4.6	SS	Yes
Foulks et al, 1979	32	5.7	SS	Yes
Perl et al, 1981	36	4.17	SS	No
Heidemann et al, 1985	66	5.8	SS	Yes
Perlman, 1981	104	4.6-5.8	SS & OS	No
Perl et al, 1981	47	6.44	OS	No
Davison & Bourne, 1981	33	4.1	OS	No
Binder, 1984	117	3.0	OS	No
Troutman et al, 1984	74	4.4-5.1	OS	No
Insler et al, 1987	31	3.9	OS	Yes
Heidemann et al, 1985	86	5.2	OS	Yes
Binder, 1988	188	3.4	OS	No
Foulks et al, 1979	32	3.5	OS	Yes

§ mean keratometric astigmatism 1 year or more postop in most studies. References to remaining authors can be found in Binder, 1985a

SS = Same size donor / recipient; OS = Oversize donor / recipient

Graft diameter

Most corneal surgeons use trephines in the range of 7.0 to 8.5 mm. The effect of different graft diameter sizes on postkeratoplasty astigmatism has been found not to be contributory to astigmatism (*Troutman & Meltzer,* 1972; *Troutman,* 1979)

Eccentric placement of donor tissue

In one study (*van Rij et al,* 1985), the astigmatism produced by grafts placed centrally was compared with the astigmatism produced by grafts placed eccentrically. A significantly greater mean astigmatism was found for the eccentric grafts but no conclusion could be made for the mechanisms of this.

The use of IOL

In PKP and IOL exchange for pseudophakic bullous keratopathy, a posterior chamber IOL sutured to the sclera is an alternative technique. Evidence from clinical and eye bank model observations is that the transclerally sutured IOLs may have an effect on early postkeratoplasty astigmatism by distorting the corneal wound at the time of keratoplasty (*Hardten et al,* 1993).

Suturing technique

The corneal sutures used for stabilisation of the donor tissue in place may be continuous or interrupted or a combination of the two. This depends on the surgeon's preference and may be influenced by the original pathology. The most commonly used techniques for suturing are multiple interrupted sutures (*Stainer et al,* 1982), interrupted sutures combined with a single running suture (*Feldman & Brown,* 1987), a single running suture (*Brown & Tragakis,* 1971), and double running sutures in opposite (*Troutman,* 1974), or same direction (*McNeill & Kaufman,* 1977).

Suture induced astigmatism can result from misplaced cardinal sutures initially, or from irregularly placed sutures in location, depth, length and tension (*Olson,* 1988). The interrupted sutures technique has the advantage of allowing selective suture removal when astigmatism is high at certain locations. The technique was first developed based on the theory that for the first 12 months following keratoplasty the cornea will assume a different curvature after selective suture removal (*Binder,* 1985a). Although *Musch et al.* (1989) have reported favourable astigmatic results with this technique compared to the double continuous suturing, *Heidemann et al.* (1985) had found increased astigmatism. In the double running suture technique by using two continuous sutures of different calibre, the purpose is to reduce distortion of the graft caused by torque. The technique has also been related with earlier visual rehabilitation (*McNeill & Kaufman,* 1977; *Davison & Bourne,* 1981). *Assil et al.* (1992), in a retrospective study have found significantly less keratometric cylinder with the double continuous suturing compared to the combined (interrupted + continuous) suture wound closure.

However, there is no general agreement that the suturing technique itself is important in final astigmatism. The amount of residual astigmatism appears not to be altered significantly by the type of suturing technique used in a number of studies (*Troutman & Meltzer,* 1972; *Jensen & Maumenee,* 1974; *Boruchoff et al,* 1975; *Troutman,* 1979; *Perlman,* 1981; *Stainer et al,* 1982). An experimental study in rhesus monkeys, suggested also that the final astigmatism after PKP is not created by suture placement or tension (*van Rij & Waring,* 1986). This view is shared by other investigators as well (*Troutman,* 1979; *Olson,* 1983).

It is however reasonable to say that the suturing itself affects the healing rate and the final curvature in a particular meridian (*Olson,* 1983). The clinical evidence from cataract operations is that sequential suture removal affects the final corneal curvature. In the CTFS it was found that the use of interrupted suturing was associated with increased astigmatism (*Bradley et al,* 1993). The position of sutures asymmetrically, not at equal depths and with variable tension, may create areas of wound gape or compression or faulty apposition of the surfaces, that may affect local wound healing (*Troutman,* 1972; *Casey et al,* 1974; *Olson,* 1983).

Wound override and dehiscence may also result from poor placement or early removal of the suture (*Brown & Tragakis,* 1971; *Boruchoff et al,* 1975).
The differing results in the literature and the lack of big prospective randomised studies with adequate follow up, represent a difficulty in interpreting results and arriving at useful conclusions.

Irregular donor recipient wound apposition

It has been suggested by *Lang et al.* (1986), that donor-recipient wound edge irregularity is responsible for the excessive astigmatism following PKP. In this clinicopathological study of 30 eyes who had undergone PKP, wound abnormalities were correlated with the presence and degree of astigmatism. Eyes with more severe astigmatism (>5 D) displayed more frequent Bowman's layer incarceration than eyes with less than 3 D of astigmatism.

Intraoperative keratometry

Troutman et al. (1977), introduced qualitative intraoperative keratometry to reduce the postoperative astigmatism. But quantitative keratometers are not accurate in keratoplasty, both in regard to dioptric power and axis of astigmatism (*Troutman,* 1987). In a comparative study, *Troutman et al.* (1984) found that the use of qualitative surgical keratometer intraoperatively, did not result in reduction of the final astigmatism after removal of all sutures.
Better results in keratoconic patients with the use of intraoperative keratometry have been reported (*Belmont et al,* 1993). At present there is no conclusive evidence that suture adjustment at the time of surgery leads to a reduction of either suture-induced or surgically induced astigmatism (*Swinger,* 1987).

1.5.4. Control of postkeratoplasty astigmatism

The amount of final resulting astigmatism after an otherwise successful PKP, is related to the different stages of the operation itself as well as to the attempts of the surgeon during the immediate or late postoperative period to reduce the corneal astigmatism by different methods.

1.5.4.1. *Prevention of postkeratoplasty astigmatism*

Prevention refers to the perioperative measures that each surgeon takes, irrespective of his personal preferences on the size of the graft to be used, the disparity to the host or the original patients pathology. Prevention of surgically-induced astigmatism is a high priority for corneal transplantation surgeons (*Coster*, 1991).

1.5.4.2. *Early control of postkeratoplasty astigmatism*

This can be achieved with one of the following methods.

1) **Selective suture removal** : The selective removal of interrupted non-absorbable sutures (*Pradera et al*, 1989; *Stainer et al*, 1982; *Binder*, 1985a; *Feldman & Brown*, 1987; *Burk et al*, 1988; *Harris et al*, 1989) is a simple way to reduce postoperative astigmatism after PKP, as any compressive effect of the suture which causes steepening of its meridian, will be released. In most instances it is advisable the removal of sutures to be performed after the wound is reasonably healed. The use of a running 11-0 suture ensures maintenance of the wound if interrupted sutures have to be removed early. The decision upon which sutures have to be released, is based on refraction, keratometry, keratography (*Harris et al*, 1989) or corneal topography (*Strelow et al*, 1991). Although the steep meridian is usually in the direction of the tight suture, this is not always the case, as sutures effect on the cornea produce force vectors (*Swinger*, 1987).

2) **Suture adjustment** : A single continuous suture can be adjusted intraoperatively or postoperatively to redistribute the suture tension away from the steep areas. The suture is adjusted by pulling from the flat to the steep meridian, resulting in tightening of the suture in the flat meridian and loosening it in the steep (*McNeill & Wessels*, 1989; *Lin et al*, 1990b; *Van Meter et al*, 1991).

It must be emphasised however that whichever suturing technique is employed, nylon sutures biodegrade over 1 to 5 years, resulting in loose or broken sutures that require removal (*Frueh et al,* 1992a). As a result, corneal astigmatism may change unpredictably and by large amounts when all remaining sutures are removed more than one year after penetrating keratoplasty, independently of the suturing technique used (*Mathers et al,* 1991; *Mader et al,* 1993). In contrast to that, another study using the selective suture removal technique (*Binder,* 1985a) has suggested that the cornea is fixed in position by 12 months postkeratoplasty, and sutures removed after that point do not change corneal curvature.

1.5.4.3. *Late control of postkeratoplasty astigmatism*

1.5.4.3.1. Refractive correction of astigmatism

Only minor astigmatic errors can be managed using spectacles, as cylinders in spectacles produce distortion (meridional aniseikonia), a problem more often appearing in elderly patients. Meridional magnification produces monocular distortion of the retinal images manifested by tilting lines or altered shapes of objects; this clinically significant problem occurs only under binocular conditions (*Guyton,* 1977).

Contact lenses may successfully correct larger cylinders, serving to reduce both aneisokonia from high myopia and meridional magnification from large degrees of astigmatism as well as aphakia (*Cowden,* 1980; *Dangel et al,* 1983; *Mannis,* 1986). They can also be used to compress or mould low rigidity grafts or realign partially everted grafts (*Ruben,* 1975; *Wilson et al,* 1992b). Different types of contact lenses can be used in postkeratoplasty corneas. Soft lenses can be beneficial in some cases, if corneal astigmatism is minimal (*Smiddy et al,* 1992). Rigid contact lenses, either gas permeable (RGP) or standard PMMA lenses can correct higher degrees of irregular corneal astigmatism (*Genvert et al,* 1985; *Mannis et al,* 1986). RGP lenses can be used as early as 4 months following PKP (*Mannis et al,* 1986; *Beekhuis et al,* 1991). However, more than 5 D of corneal astigmatism can be successfully treated with RGP lenses in only 16% of patients (*Smiddy et al,* 1992), whereas astigmatism greater than 12 D virtually precludes successful conventional RGP lenses fitting (*Beekhuis et al,* 1991). Scleral contact lenses (*Daniel,* 1976) and triangular lenses (*Diamond et al,* 1992) have also been tried to improve lens stability, but with moderate patients tolerance.

Contact lens use is not devoid of complications. Problems often arise as a consequence of lens instability especially with hard lenses (*Treumer,* 1986); superficial neovascularization especially when sutures are still present (*Mannis & Matsumoto,* 1983; *Dangel et al,* 1983); infection or graft rejection (*Cavanagh & Leveille,* 1982; *Genvert et al,* 1985). Corneal grafts exhibit reduced sensitivity (*Ruben & Colebrook,* 1979). Although this may improve lens tolerance, it may also delay presentation of lens-induced complications. Additionally, many elderly patients are unable to tolerate or handle contact lenses. The use of extended wear lenses is associated with more problems than other types of lenses (*Mannis,* 1986). The percentage of all patients undergoing PKP who are eventually fitted with contact lenses for refractive purposes varies in different series, from 10% (*Jensen & Maumenee,* 1979) to 16% (*Smiddy et al,* 1992). For PKPs performed at Bristol Eye Hospital, this percentage was 6.5% for the decade 1981-91 (*Diamond et al,* 1992).

1.5.4.3.2. <u>Surgical control of late postkeratoplasty astigmatism</u>

Surgical intervention is considered when optical means fail to provide adequate visual rehabilitation. In a report from Moorfields Eye Hospital, 18% of 201 grafts for keratoconus required refractive surgery for disabling high astigmatism (*Kirkness et al,* 1990 and 1991). At Flinders Medical Centre of South Australia, 8% of all the performed corneal grafts end up having relaxing incisions for postoperative astigmatism (*Coster,* 1991). Other authors estimate the incidence of disabling astigmatism requiring refractive surgery for correction, as 10%

(*Laroche*, 1987). Of the cases followed up in the *Australian Corneal Graft Registry* (1989), 3% required refractive surgery.

History of surgical correction of astigmatism

Bates (1894) was among the first to propose transverse keratotomy incisions to correct astigmatism, although he himself did not follow through with any surgical cases (*Waring*, 1989b). Reportedly, the first surgeon to use incisions for the correction of astigmatism, was *Lucciola*, in Italy in 1896, whereas in 1898 *Lans* published an extensive series of experiments on rabbits with corneal sections and cauterization to reduce astigmatism. In the 1940's and 1950's Professor *Sato* in Tokyo performed anterior and posterior incisions using a special knife, both radial and transverse for myopia and astigmatism. He managed to reduce the astigmatism in a series of 15 eyes an average of 2.50 D. In the 1970's several surgeons in the former Soviet Union (Krasnov, Durnev, Yanaliev, Fyodorov) utilised non-perforating anterior keratotomies for the correction of myopic astigmatism. Their techniques were adopted by surgeons in the United States beginning in 1978 (*Lindstrom*, 1990).

Theory

The various surgical techniques to eliminate astigmatism can be classified into three different approaches. The first approach produces its results mainly by relaxing the steep corneal meridian, and includes the various types of relaxing incisions (parallel, arcuate, trapezoidal and transverse). Suture release although not a surgical procedure per se, produces its effect in a similar way. The "tissue relaxation principle" explains the effect of these procedures. An incision in the cornea relaxes tissue and because of the consequent spread of tissue, all unsutured incisions act as if tissue is added. This effectively increases the arc length of the cornea in the operated meridian causing flattening and reduction of the meridional power. The effect depends on the position, length and depth of the incision (*Rowsey,* 1983; *Swinger,* 1987; *Thornton,* 1994).

The second approach causes steepening of the flat corneal meridian by compression. Techniques in this group include semilunar (crescentic) resection, corneal wedge resection, corneal tuck (compression sutures) and wound revision. *van Rij & Waring* (1984), studied experimentally the mechanisms involved in compressive procedures, and came with the "tissue compression theory" suggesting that a wedge resection or placement of an anterior corneal suture compresses the tissue focally, depressing the cornea locally but steepening it centrally.

Finally, a combination of two approaches can be used, such as relaxing incisions with compression sutures, to enhance the effect of the procedure.

These procedures can be used in different causes of astigmatism [Table 1.8]. For the purpose of this thesis however, only the procedures that are used in postPKP astigmatism will be discussed further.

<u>**TABLE 1.8**</u> : Refractive procedures for surgical control of astigmatism.

Procedure	Congenital astigmatism	Post-cataract astigmatism	Post-PKP astigmatism
<u>**Relaxation**</u>			
Suture release	-	✓	✓
Parallel keratotomy	rarely	rarely	-
Arcuate keratotomy	rarely	rarely	✓
Trapezoidal keratotomy (Ruiz)	✓	✓	rarely
Transverse keratotomy (T cuts)	✓	✓	✓
<u>**Compressive**</u>			
Semilunar (crescentic) resection	✓	-	-
Wedge resection	-	-	✓
Corneal tuck (compression sutures)	rarely	rarely	rarely
Wound revision	-	✓	✓
<u>**Mixed**</u>			
Relaxing incisions+Compression sutures	-	rarely	✓

The coupling effect: relationship between incised and unincised meridians

The term "coupling effect" refers to the changes in curvature that occur in the incised meridian and at the same time in the orthogonal (90^{o} away) unincised meridian. It is closely related to the fact that the perimeter of the corneal curvature (limbus) remains constant. When an incision induces flattening in the 90^{o} meridian, there should be an equal compensatory steepenning in the 180^{o} meridian. This is known as the flattening/steepening ratio (F/S) or coupling ratio. When the amount of flattening to steepening are the same, there is no change in the spherical equivalent (*Thornton,* 1994).

A. <u>Relaxation procedures</u>

1. Relaxing incisions (paired arcuate keratotomies)

With this technique two incisions made opposite to each other within the graft-host interface or few millimetres central to it, in the steep corneal meridian (the meridian parallel to the plus cylinder refraction axis), act to flatten that corneal meridian. Each incision is extended over 60^{o} to 90^{o} and made to a least 75% of the corneal depth. The technique was first described by *Troutman & Swinger* (1980) for the correction of high postkeratoplasty astigmatism, and was then popularised by other surgeons (*Krachmer & Fenzl,* 1980; *Sugar & Kirk,* 1983; *Lavery et al,* 1985). Surgery is done either at slit lamp microscope or in operating room. The coupling effect with this technique was calculated 0.975 by *Sugar & Kirk* (1983), with a negligible change in spherical equivalent (*Lindstrom & Lindquist,* 1988; *Lindtsrom,* 1994), but varying the length of the arcuate incisions give different effects (*Lundergan & Rowsey,* 1985). One of the advantages of the method is that the correction is stable after a relatively short period of time (*Krachmer & Fenzl,* 1980), but its major disadvantage relates to its unpredictability (*Lavery et al,* 1985; *Lindstrom & Lindquist,* 1989; *Lindstrom,* 1994).

2. Trapezoid relaxing incisions (Ruiz procedure)

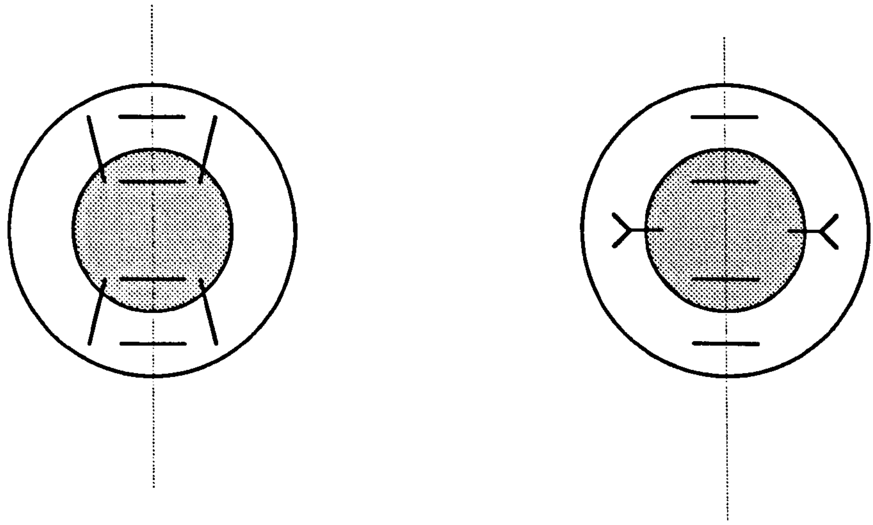


Figure 1.4A (left): Ruiz procedure and **Figure 1.4B** (right): modified Ruiz procedure with compression sutures. Dotted line indicates steep meridian.

The method of trapezoidal relaxing incisions for the correction of idiopathic astigmatism was first developed by Louis Antonio Ruiz of Bogota, Colombia. This procedure involves the creation of 4 equally spaced tangential incisions and 2 semiradial incisions on each side of the steep axis [figure 1.4A]; variable optical zone sizes are used to alter the amount of correction. The procedure can also be used in combination with compression sutures placed across the wound in the flat axis [figure 1.4B]. The use of this method in the correction of post-PKP astigmatism has been reported in the past (*Lavery et al,* 1985; *Merck et al,* 1986; *Maxwell & Nordan,* 1986; *Arffa,* 1988). The procedure is unpredictable but also, semiradial incisions carry an increased risk of perforation when they cross the keratoplasty wound, and poor healing has been observed after these incisions (*Deg & Binder,* 1987). Because of these problems the technique has now largely been abandoned in treating postkeratoplasty refractive errors (*Lindstrom,* 1994).

3. Transverse keratotomies (T cuts)

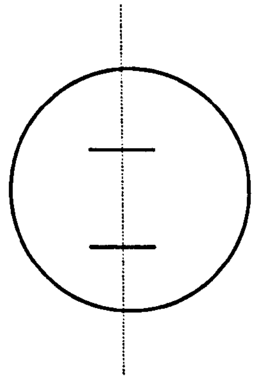


Figure 1.5

Some surgeons use a single, or sometimes double pair of transverse incisions placed across the steep corneal meridian. The effect of the incisions is to flatten the steep meridian to the same degree that they steepen the flat meridian. There is a variable response by varying the length and position of transverse cuts. These keratotomies are typically indicated for the correction of low degrees (1-3 D) of naturally occurring astigmatism. Clinical results in 124 patients reported by several surgeons showed a mean astigmatic correction of 1.58 D from a single pair of transverse incisions placed 5 to 8 mm apart (*Lindstrom & Lindquist*, 1989). *Maguire & Bourne* (1989b) and *Saragoussi et al.* (1992) have used the technique in post-PKP patients but experienced poor predictability.

B. Compressive procedures

1. Compression sutures (corneal tuck)

One to four 10/0 nylon sutures placed across the host-donor interface on opposite sites of the graft, without making any incision, act to steepen that corneal meridian and have been used for the reduction of post-PKP astigmatism (*Limberg et al*, 1989). Nevertheless, the technique in post-PKP corneas has been unpredictable (*Price & Whitson*, 1991), whereas astigmatism cannot be permanently corrected with compression sutures alone.

2. Wedge resection

A wedge resection in the flat axis acts like tension sutures by steepening this meridian (*van Rij & Waring,* 1984). The overall effect of wedge resection is to steepen the flatter meridian approximately twice as much as it flattens the steeper meridian. The net effect is an increase in myopia or decrease in hyperopia (*Lindstrom & Lindquist,* 1989). The general rule is that the anterior size of the removed wedge should equal approximately 0.1 mm for each diopter of desired astigmatic change (*Olson,* 1988), although *Lindstrom & Lindquist* (1988) estimated that resection of 0.10 mm of tissue results in approximately 2 D of astigmatic correction. After the removal of excess corneal tissue, five to seven deep and evenly spaced interrupted sutures are placed. The sutures must be left in place for a long time, and the wound is not stable for at least 6 months postoperatively (*Olson,* 1988). The procedure is technically difficult to perform, especially the second incision since the cornea is more flaccid as a result of the first incision (*van Rij & Vijfvinkel,* 1983), and quantify, and is therefore now rarely used, reserved for pronounced amounts of astigmatism. Wedge resection technique is used for correction of large amounts of cylinder, up to 20 D of astigmatism (*Lindstrom,* 1994). Unresolved problems of the method, are the unpredictability (*van Rij & Vijfvinkel,* 1983; *Lugo et al,* 1987; *Olson,* 1988; *Frucht-Pery,* 1993) and the long waiting period to achieve stability.

3. Wound revision

Simple wound revision may be indicated in cases where the graft overrides the recipient bed (uplift) or a small wound dehiscence occurs. The incision is simply debrided, dissected open and resutured. The effect and visual recovery is similar to wedge resections because of the multiple sutures (*Lindstrom,* 1994).

C. Mixed procedures

Relaxing incisions and compression sutures

A combination of relaxing incisions with compression sutures (augmented relaxing incisions) can be used to increase the amount of correction achieved with arcuate relaxing incisions alone. The placement of compression sutures at both poles of the unoperated (flat) meridian increases the effect of relaxing incisions by causing further gaping of the relaxing incision during healing (*Swinger,* 1987). The method has been used by different surgeons in post-PKP astigmatism correction, with variable results (*Mandel et al,* 1987; *McCartney et al,* 1987; *Lustbader & Lemp,* 1990; *Frangieh et al,* 1991; *Whitehouse et al,* 1994; *Jacobi et al,* 1994)

1.5.4.3.3 Thermal cautery (thermokeratoplasty procedures, TKP)

Thermal cautery with a bipolar scleral diathermy or a holmium laser is another approach for reduction of astigmatism. The technique of bipolar scleral diathermy has been applied at the limbus or at a distance of 1 mm in 12 eyes with congenital, post-cataract and postkeratoplasty astigmatism (*Treumer & Johnigk,* 1991). A mean decrease of 7.8 D was primarily achieved followed by a regression of 3.7 D within the third post-operative month. Infrared Ho:YAG laser (2.06 μm) and deep stromal hot needle thermocoagulation have also been tried in early clinical evaluations in arcuate applications in flat meridians of eyes with naturally occurring hyperopic astigmatism (*Neumann et al,* 1991) and only one post-PKP eye (*Hennekes,* 1995), but wide clinical application on post-PKP corneas is yet to be tried.

1.5.4.3.4 Laser treatment (Photoastigmatic Refractive Keratectomy, PARK)

Transverse linear laser keratectomy (T incisions) via a mask, has been used as an alternative to diamond knife incisions in naturally occurring astigmatism (*Seiler et* *al,* 1988) with disappointing results (*Schipper et al,* 1994). Toric ablations using expanding slits with rectangular aperture elements have also been used for the correction of regular myopic astigmatism (*McDonnell et al,* 1991; *Spigelman et al,* 1994) with better results. Excimer laser use has also been reported for the correction of postkeratoplasty astigmatism (*Campos et al,* 1992; *Gibralter & Trokel,* 1994; *Lazzaro et al,* 1996; *Amm et al,* 1996; *Tuunanen et al,* 1997) in a few patients so far. The early results however are not any better than conventional surgical treatment. PARK could correct only the regular astigmatic component of the grafts, but it carries the disadvantage of substantial regression (*Campos et al,* 1992), hyperopic shift (*Amm et al,* 1996) and severe late developing of corneal haze (*Tuunanen et al,* 1997).

1.6. OBJECTIVES AND OUTLINE OF THIS THESIS

The work presented in this thesis, has the aim to investigate various aspects of the problem "post-keratoplasty astigmatism", and look into ways of better evaluation, early control and its late treatment, with the aid of computer assisted video-keratography.

The work is divided into four main studies, each one having a different objective.

The first study (chapter 2) deals with the evaluation of measurement agreement and measurement variability (intra- and inter-observer) for the keratometer and for the TMS-1 videokeratography instrument, on both normal and post-keratoplasty corneas. Postkeratoplasty corneas are expected to be highly astigmatic, and the performance of the two instruments might be different under these clinical conditions.

The second study (chapter 3) has the objective of creating a clinically useful qualitative classification of computer generated topographic maps in post-keratoplasty corneas. Also, to correlate patterns to preoperative diagnoses or keratometric and refractive data. There is a need for such a classification, because of the inadequacy of the classifications used for normal corneas, to cover for the variety of patterns seen in post-PKP populations.

The task of the third study (presented in chapter 4) is to answer the question of suture induced post-PKP astigmatism by comparing the astigmatic results induced by two different suturing techniques currently used by eye surgeons in corneal grafting. The two comparable techniques are: (a) a single continuous 10/0 nylon suture (SCAS) adjustable postoperatively to regulate astigmatism and (b) a combination of a continuous 11/0 nylon suture and 12 interrupted 10/0 nylon sutures (ICS) which are removed selectively after the operation to reduce astigmatism. The study presented in this thesis is a prospective randomised one and the assessment of astigmatism was performed with computer assisted corneal topographic analysis.

In the fourth study (chapter 5), a prospective case controlled randomised trial has the task of assessing the effectiveness of CAVK in refining the plan for surgical correction in cases with high astigmatism following penetrating keratoplasty. CAVK carries the theoretical advantage over keratometry and refraction in obtaining more information on corneal contour. Whether this will improve predictability of postkeratoplasty refractive surgery remains to be seen.

Chapter 6 is a general final discussion of the conclusions of this thesis and proposals for further work.

CHAPTER 2

MEASUREMENT AGREEMENT AND REPEATABILITY OF KERATOMETRY AND COMPUTER ASSISTED VIDEOKERATOGRAPHY ON NORMAL AND ASTIGMATIC CORNEAS

2.1. Introduction

Measurement is a scientific method used in every aspect of clinical or experimental medicine. The *accuracy* of a method refers to how close the measured values are to the real value. *Precision* refers to the agreement between repeated observations; this concept is also expressed as *reproducibility or repeatability* of the instrument which is a more precise term describing the error involved in repeated measurements of the same parameter.

Computer assisted videokeratoscopes (CAVK) are instruments that calculate the corneal power and reproduce the corneal profile with a certain level of accuracy and precision. It is important, and clinically useful, to know the precision of these relatively new instruments, especially in comparison to the previously available "gold standard" ones such as the keratometer which follow a different methodology in corneal calculations.

A significant amount of research has taken place regarding the accuracy of CAVK devices on test surfaces, mainly calibrated test spheres, and normal corneas. These results have shown an acceptable level of accuracy and reproducibility for different commercially available models of CAVK (*Hannush et al,* 1989 and 1990; *Wilson et al,* 1992a; *McCarey et al,* 1992; *Legeais et al,* 1993; *Maguire et al,* 1993).

However, in practical clinical terms we often use both keratometry and CAVK in measuring abnormal corneas such as those seen after PKP. It would be therefore useful to know and compare the performance of these instruments not only in normal corneas, but also in postoperative, highly astigmatic corneas.

2.2. Aims of the study

This is a comparative study between the keratometer and the CAVK in terms of both measurement agreement and repeatability. It has been conducted in the form of four parallel studies in order to :

1. assess the measurement agreement between keratometry and video-keratography in normal non-astigmatic corneas.
2. assess the measurement agreement between keratometry and video-keratography in highly astigmatic postkeratoplasty corneas.
3. assess the repeatability with respect to repeated measures made by a single observer (intra-observer variability) and by two different observers (inter-observer variability) for both keratometry and videokeratography in normal non-astigmatic corneas.
4. assess the intra-observer and inter-observer variability for both instruments in astigmatic postkeratoplasty corneas.

For all these studies, evaluation was conducted in terms of dioptric power and axis of the two principal corneal meridians, as well as magnitude of corneal astigmatism.

2.3. Materials and methods

2.3.1. *Instruments*

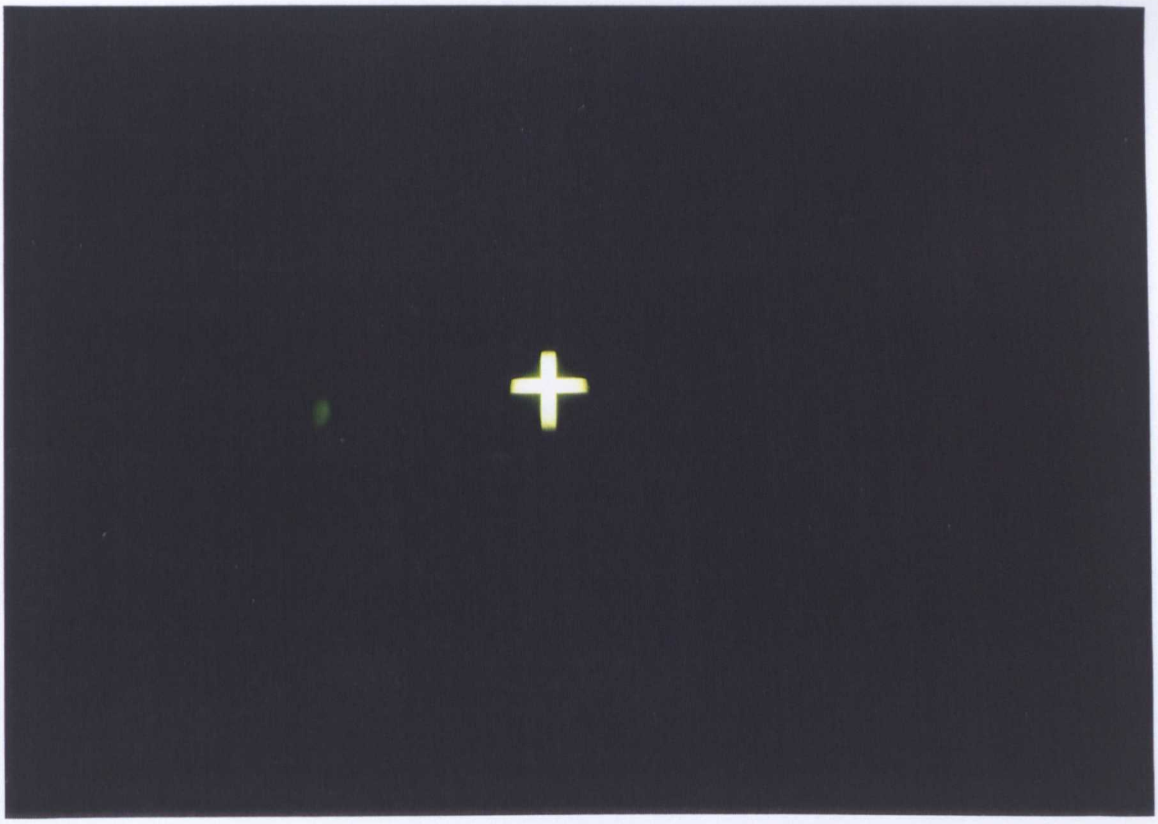
2.3.1.1. Keratometry

The keratometer used in this and the following studies was the 10 SL/O model of Carl Zeiss Ltd. This is applied as an attachment to the Zeiss slit lamp [figure 2.1]

Specifications

The 10 SL/O model is an ophthalmometer after Helmholtz and follows the variable doubling principle of operation. The measured range of the instrument for radii of curvatures is from 4.00 to 11.2 mm, with a scale interval of 0.01 mm. The measured corneal diameter is from 1.5 to 3.5 mm depending on the radius of the examined cornea. The scale accuracy throughout the entire measuring range is ± 2×10^{-2} mm. This is within the recommended tolerance for keratometers (*Stone*, 1962). The calibration accuracy of the instrument is ± 0.5×10^{-2} mm, with the measured value display unaffected thermally. The magnification of the

Figure 2.1 : Close-up photograph of the 10 SL/O model keratometer (Carl Zeiss Ltd.). The system is applied as an attachment to the Zeiss slit lamp.



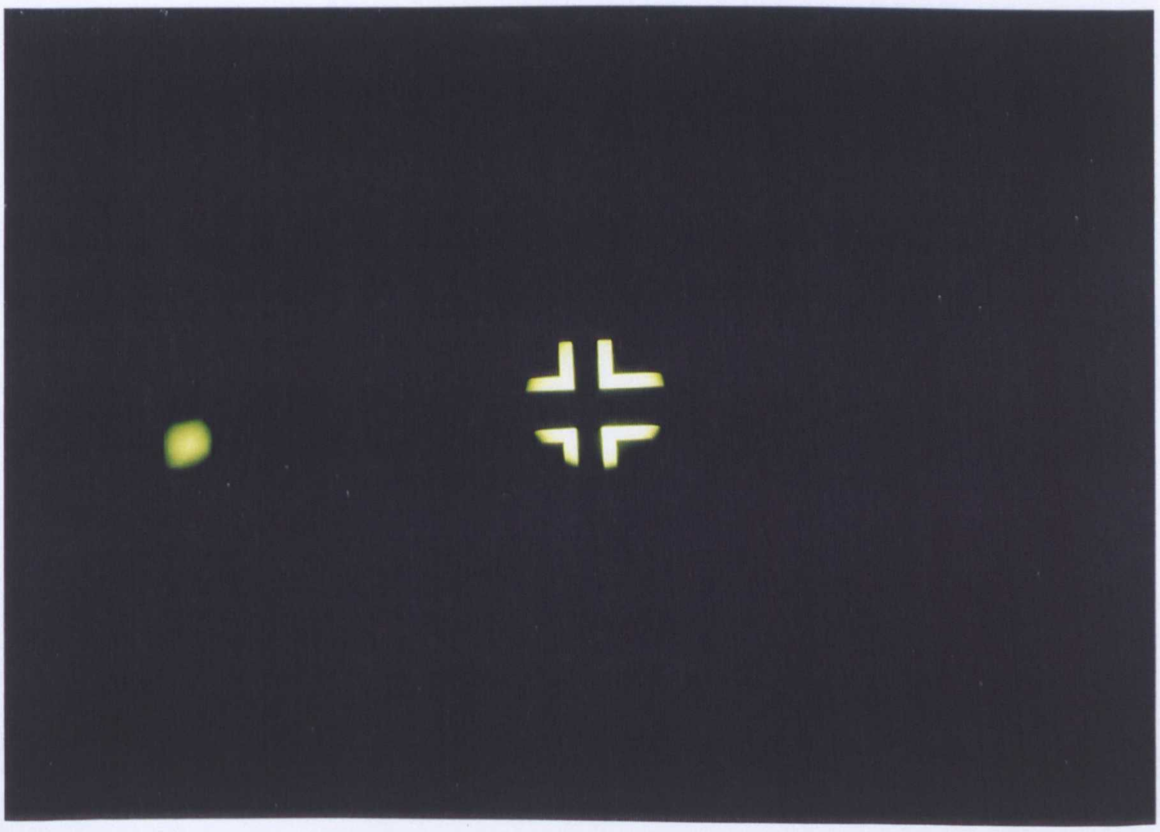


Figure 2.2A (top) and 2.2B (bottom) : The Zeiss keratometer mires. Readings are obtained when adjustment of the solid cross into the hollow cross occurs.

ophthalmometer eyepieces is 20x (*Carl Zeiss Inc. keratometer*, 1989).

Mode of operation

The instrument is designed to measure toroidal surfaces in the two principal meridians. For this purpose the mires are rotatable 180^{o} about the optical axis until their images appear no longer distorted. It is impossible to obtain a correct alignment of the doubled images unless the mires are situated along a principal meridian. After identifying the radius of curvature of one principal meridian, the mires [figures 2.2A & 2.2B] are rotated to locate and measure the other meridian which will be at an angle other than 90^{o} if the astigmatism is irregular. The Zeiss ophthalmometer is therefore a "two position" instrument (in contrast to "one position " instruments like the Bausch and Lomb which measure both meridians at one location), and can thus measure principal corneal meridians that are not perpendicular.

The instrument does not provide direct reading of the dioptric power of the cornea at the meridian under examination. However, the scale for reading radii of curvature R, can be transformed to surface power according to the keratometric formula.

2.3.1.2. Computer assisted videokeratography

For the purpose of these studies, the TMS-1 (Computed Anatomy, New York, NY[1], software version 1.61) model of corneal topography was used [figure 2.3]. The instrument follows the general principles of CAVK as discussed in the general introduction. This particular model has the following characteristics.

Number of rings and corneal coverage of the target

The topographic monitoring system (TMS-1) projects 25 or 32 rings of cool green light onto the cornea from a cylindrical Placido through a light cone at a distance of 32 mm from the 12th ring (*Wilson et al*, 1992a). The low luminosity light cone of the TMS-1 eliminates problems in testing photophobic patients. The central

[1] Later, the TMS-1 became available from Tomey Technology, Cambridge, Massachusetts

ring of the Placido cone has a diameter of 0.48 mm. The patented photo-keratoscope (US patent #4,772,115) presents data from apex to limbus when using the 32 rings cone version, whereas the corneal coverage with the 25 rings is smaller. The TMS-1 model that was used throughout this and the following studies, was operating on a 25 ring cone as supplied by the manufactures [figure 2.4]. With such a cone, for a 42 D cornea the diameter of the measured zone is 0.4 to 8.9 mm. The range of radius of curvature that can be measured with the instrument is 33.75 to 3.38 mm, corresponding to a 10 to 100 D range of corneal power (*Corneal Modelling System,* 1989).

Working distance and focusing of the instrument

The system uses a short working distance, approximately 40 mm distance from the surface of the eye to the effective plane of the Placido source. The patient fixates a light centred in the cone and focusing of the instrument is done by manoeuvring the Placido target with a joystick. The TMS-1 employs a patented laser focusing system. Two low-power HeNe laser sources (Class II laser) are used to produce spots which must be criss-crossed precisely 160 microns within the stroma to achieve proper focusing (crossed laser apex focusing system) (*Mammome et al,* 1990). However, the machine itself does not provide any record or verification of proper focusing. The alignment is again joy-stick operated with a provided record in terms of left/right and up/down alignment.

Optical system and videocamera

There is an integrated high-magnification fully coated camera lens with field of view of 10 x 13 mm viewable on an internal monitor or 11 x 14 mm video signal. The image is captured by a CCD digital video camera which has a resolution equivalence of approximately 1500 x 1000 pixels. The camera is able to convert the image into a 512 by 512 array of numbers representing the intensity of light at corresponding points in the original image, and is this array of so-called pixel values which must be evaluated automatically by computer (*Klyce & Wilson,* 1989).

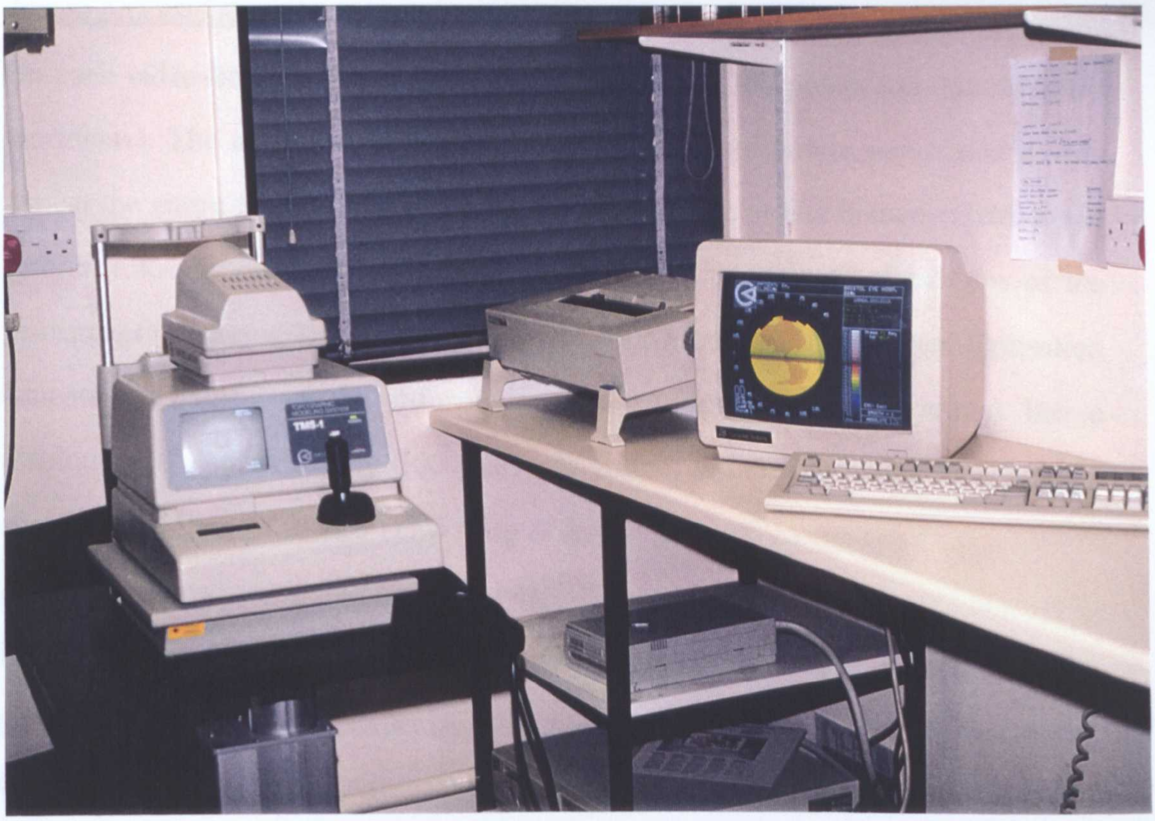


Figure 2.3 : The TMS-1 system.

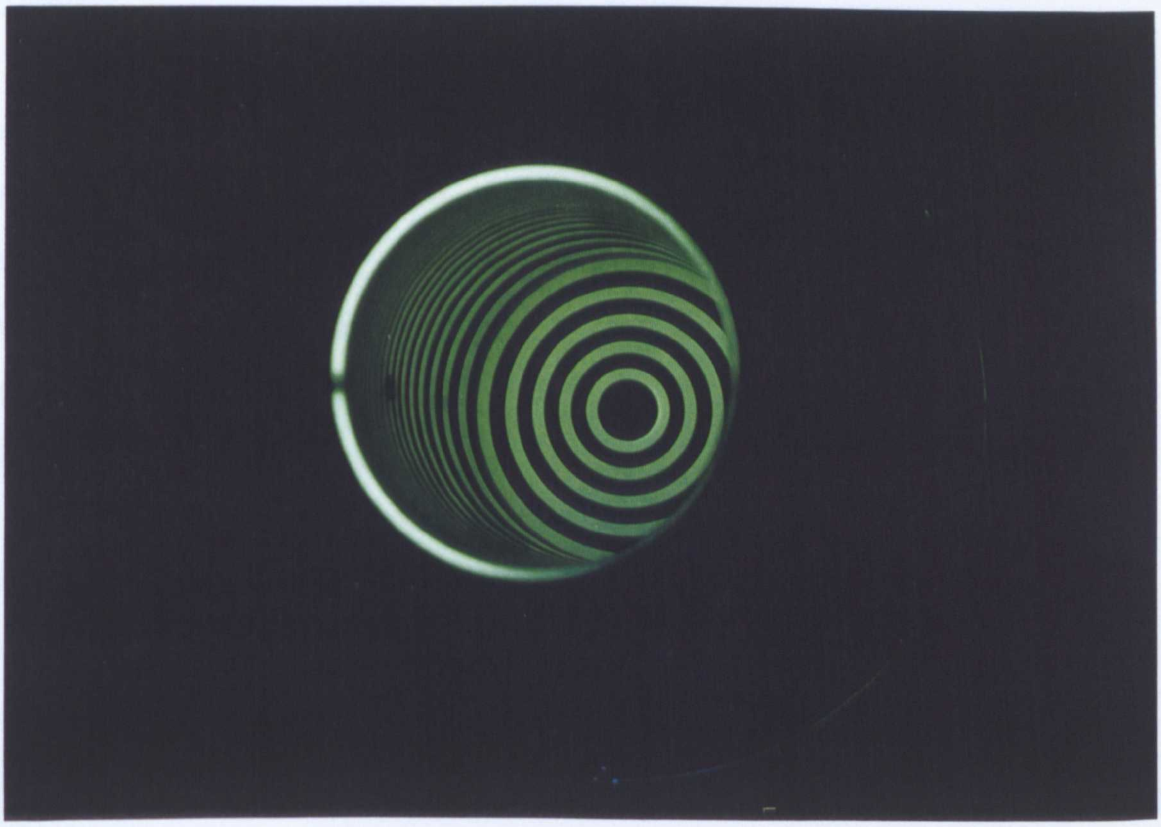


Figure 2.4 : Close up photograph of the low luminosity 25-ring cone of the TMS-1 system.

Image processing

On each video-keratoscope ring the TMS-1 evaluates 256 points (on 256 different meridians). The total analysis includes 7,000 individual power points and covers almost the entire cornea. The location of these specific points is then calculated in reference to a known calibration file provided by the patented algorithms of the instrument (Datamap® software). The operator-monitored automated digitisation (statistical analysis of the information by the computer's algorithms) has a resolution of approximately 500 lines per frame, which correlates to a corneal surface resolution of ± 0.20 D (*Wilson & Klyce,* 1991a).

Storage options

Multiple storage options of the information are available. These include the video processing unit's (VPU) hard disc, floppy discs, or removable 90Mb or 150Mb optic (Bernoulli) discs. All examinations performed throughout this and the following studies were stored on floppy or Bernoulli discs.

Displays

The TMS-1 provides a variety of interpretational displays and interactive surface maps. Here only the corneal statistics provided by the machine's software that are relevant to the current study are described. In the materials and methods section of the following chapters 3, 4 and 5 other forms of information displays relevant to the other studies, are described.

Corneal statistics

Simulated keratometry (simk) value

This is an index that provides the power and location (axis) of the steepest meridian as well as power and axis of the meridian 90^{o} away for 128 equally spaced meridians (*Wilson & Klyce,* 1991b), from a reconstructed surface corresponding to the area measured by the keratometer. These values are obtained from power points on the photokeratoscope rings 7, 8 and 9. These mires were selected by the manufacture company because their position on the corneal surface approximates the location at which standard keratometry is obtained. The instrument also provides the *non spherocylindrical simK value*, which is the power and axis of the flattest meridian regardless of the angle between the steepest and flattest meridian. Corneas with regular astigmatism have spherocylindrical and non spherocylindrical simK of very similar value. In the case of corneas that show irregular astigmatism, the steepest and flattest meridians are separated by an angle other than 90^{o} and there is difference between the spherocylindrical simK and the flattest meridian. In this study the non spherocylindrical simk value was used in all calculations.

Surface Asymmetry Index (SAI)

This is a quantitative descriptor of the corneal shape developed initially by *Dingeldein et al.* (1989) on the LSUCTS and later adopted by the commercially available TMS-1 (*Wilson & Klyce,* 1991b). This index called Surface Asymmetry Index (SAI), is a centrally weighted summation of differences in corneal power between corresponding points 180^{o} apart on 128 equally spaced meridians that cross the four central photokeratoscope mires (*Dingeldein et al,* 1989; *Klyce & Wilson,* 1989; *Koch et al,* 1989). For example if the power on ring 4 at 90 degrees is 44 D and the power of ring 4 at 270 degrees is 45 D, the difference of 1 D between the two powers is entered into the summation of the computer, and so on. Therefore, SAI approaches zero for a perfectly spherical surface, a surface with perfectly spherocylindrical regular corneal cylinder, or for any surface with a power that is radially symmetrical and increases as the shape becomes more asymmetric (*Dingeldein et al,* 1989).

Surface Regularity Index (SRI)

This is a quantitative index determined from the summation of local fluctuations in power along 256 equally spaced semimeridians on the central ten photokeratoscopic mires. The SRI is centrally weighted (for the Stiles-Crawford effect), and analyses that portion of the cornea that corresponds approximately to the area of the entrance pupil under standard luminosity conditions. This virtual pupil is approximately 4.5 mm in diameter (*Wilson & Klyce,* 1991b). The SRI approaches 0 for a normally smooth corneal surface and increases as irregular astigmatism increases.

2.3.2. *Patients*

For the normal population study, both corneas from 17 normal subjects (9 females) aged 18 to 64 years (mean 36 yr.) were studied. All normal subjects studied were either doctors, nurses, clerical staff working at Bristol Eye Hospital, or individuals accompanying patients. Corneas were considered normal and included in the normal population study, only if there was : 1) no history of ocular surgery, 2) no slit-lamp microscopy evidence of trauma or corneal disease, 3) best corrected visual acuity (BCVA) of 6/60 or better to allow adequate fixation, 4) regular keratometric readings, 5) keratometric astigmatism of < 1.50 D. Two of the 34 eyes had to be excluded from the study (one due to a central corneal opacity of unknown aetiology which produced distorted keratometric mires, and the second because of excess corneal astigmatism). This left 32 normal corneas for analysis.

For the astigmatic corneas group, 33 postkeratoplasty corneas from 27 patients (15 females) aged 19 to 92 years (mean 53.2 yr.) were examined within the study period. Preoperative diagnosis included 12 eyes with keratoconus, 9 eyes with Fuchs' endothelial dystrophy, 6 eyes with HSK, 2 eyes with aphakic bullous keratopathy, 3 eyes with various corneal dystrophies, and one eye was operated for keratoglobus. At the time of examination, all cases were within twelve months from the PKP (mean 7.1 months, range 1-12 months), as the aim of the study was to compare CAVK with keratometry in corneas with irregular astigmatism. The suturing technique used for the PKP was either a single continuous suture (24 bites 10/0 Nylon), or a combination of interrupted (12x10/0 Nylon) and continuous (12 bites 11/0 Nylon) sutures. At the time of examination, patients had a variable number and location of sutures present, or all sutures had already been removed. As with the normal population group, BCVA of 6/60 or better to allow adequate fixation with keratometry and CAVK was one of the entry criteria.

2.3.3. *Methods*

All measurements for a given instrument were made by two operators.

Examination conditions

All corneal topographic examinations were conducted in the same site. Keratometric readings were obtained in a similar room and the same keratometer was used in all cases. The rooms were kept in semi-darkness to facilitate fixation.

Calibration of the device

The 10 SL/O Zeiss keratometer had been calibrated before the start of the study and periodically checked using an accurately machined steel ball of known radius of curvature of 7.50 mm as a test surface according to the manufacturer's instructions. The patented solid-state VKS of the TMS-1 has been designed to require no field calibration. The instrument used in the study had been aligned and calibrated at the initial installation by technicians of the manufacture company on site.

Methods

Three measurements per eye for a given instrument were obtained by two independent operators. One observer made all measurements with the keratometer, while the second observer made all measurements with the TMS-1. The patients were instructed to blink and refixate, but also to avoid any head movement between measurements, as this might have led to head tilt and axis tilt. No artificial tears were used in any case. The sequence of the measurements with the two instruments was not randomised, but was not always done in the same order and the two investigators had no knowledge of the results obtained by the fellow observer.

Prior to obtaining each measurement by the keratometer, the eyepieces of the instrument were set by each investigator to correct for their refractive error if they were not wearing contact lenses or spectacles. None of the observers was wearing astigmatic correction. After patient's fixation and alignment of the mires by the examiner, the steep and flat meridians power and axis were read from the scale of the instrument. Millimetre radius readings were taken from the radius of curvature scale of the 10 SL/O keratometer (our instrument did not have the facility of direct diopter readings). A refractive index of 1.3375 was assumed for conversion from sphere radius to diopters instead of the recommended by Zeiss index 1.332, because in order to directly compare the two instruments we wanted to eliminate the bias of a non uniform keratometric index.

All three captured images with the TMS-1 were digitised and processed. Absolute scale topographic maps were obtained for each eye, and the non-orthogonal simk readings (power and axis) and SAI and SRI indices for all examinations were obtained from the instrument's display.

Data collection

All data were kept initially in forms separately from routine clinical records and were subsequently entered into an integrated spreadsheet program (Microsoft Excel, version 4.0) on an IBM computer. The notation of 0^{o} and 180^{o} meridians for cylinder axis presents a potential problem for analysis. Because the maximum possible difference in cylinder axis is 90^{o}, 180^{o} was added to, or subtracted from the difference in cylinder axis if that was greater than 90^{o}. Additionally, degrees measurements data were converted to absolute numbers to facilitate analysis.

2.3.4. *Statistical analysis*

Descriptive statistics and scattergrams of this study were obtained from the Excel (Microsoft Inc, USA-version 4.0) statistical program. Statistical calculations of the limits of agreement, confidence intervals and coefficient of repeatability were personally performed on an IBM computer.

In order to assess measurement agreement between instruments, the average of the three measurements for each examiner were considered. The differences in averaged measurements between the two instruments (y-x), were calculated and plotted against the mean of the two instruments measurements, according to the methods described by *Bland & Altman* (1986). The mean of the differences (d) represents the bias between the two instruments. The "limits of agreement" were calculated as d $\pm$ 2SD, [d=mean difference, SD=standard deviation] and the 95% confidence intervals for the bias (mean difference) calculated by d $\pm$ (t x SE), $t_{0.05,n-1}$ [SE= standard error of the mean, n-1 degrees of freedom]. Confidence intervals are intervals that with high probability contain the true difference. The difference in outcomes was considered significant at the 5% level, if the 95% confidence interval did not contain the value of zero (*Simon,* 1986). Additionally, the percentage of scores within specific ranges were determined.

Observers variability (repeatability) was similarly determined. The deviation of each measurement from the mean of the three measurements of the same observer for each cornea, was calculated for the intraobserver variation. The deviation scores were plotted against the mean of the three measurements for each subject. For the interobserver variation, the difference to the mean of observers 1 and 2 was plotted against the mean of both observers measurements (six measurements). Additionally the percentage of scores within specific ranges were determined. Statistical analysis for determining reproducibility included also calculation of the coefficient of repeatability, which is defined as twice the standard deviation of the differences (*Bland & Altman,* 1986).

2.4. Results

2.4.1. Measuring agreement between keratometry and TMS-1

For the calculation of measuring agreement between the two instruments on normal as well as astigmatic corneas, the second series of measurements with each method, performed by the same examiner was selected.

2.4.1.1. Measuring agreement between keratometry and TMS-1 on normal corneas

Power measurements

Statistical data of the results of power measurements for both instruments on normal corneas, are presented on Table 2.1. Statistically significant differences (95% confidence limits not including 0) between the two instruments was found in measuring steep and flat meridians dioptric power (D) as well as keratometric astigmatism. A systematic bias was revealed in the measurements of all these parameters. There was tendency for the TMS-1 to measure steeper than the keratometer on a consistent basis. The TMS-1 presented higher values than the SL-10 keratometer in the measurement of the steep meridian power in all 32 measurements (mean -0.68 D, SD 0.26 D). This strong bias is shown in figure 2.5A, and by the limits of agreement values and confidence intervals [Table 2.1]. For the flat meridian measurements, the TMS-1 also demonstrated a bias towards recording higher values than the keratometer in 30 out of the 32 measurements (94%) [Figure 2.6A]. The absolute mean difference was -0.41 D (SD 0.42). If 0.50 D is considered a clinically acceptable difference between the instruments, table 2.3 shows that in only 31% of the measurements of steep axis power the agreement was better than 0.50 D; this percentage for the flat meridian measurements is 56%. For a clinical agreement of 0.25 D, these percentages fall to 6.25% and 18.75% respectively. For the astigmatism magnitude, the bias again was for the TMS-1, which in 23/32 cases (72%) recorded higher astigmatism than the keratometer [Figure 2.7A, Table 2.1].

Location measurements

In 2 eyes, the keratometric astigmatism was equal to zero, and these eyes were excluded from the comparison. The measurement agreement between the two instruments was very good on both steep and flat axes location [Table 2.1]. The distribution of measured differences in axes between the two instruments compared to the measured astigmatism is seen in Table 2.4. As it could be anticipated, there was a tendency for more than 30^{o} disagreement between the two instruments in smaller degrees of astigmatism, whereas higher values of astigmatism tended to give measurement agreement better than 20^{o} [Table 2.4].

2.4.1.2. Measuring agreement between keratometry and TMS-1 on astigmatic post-PKP corneas

Power measurements

The results of the measurements are graphically illustrated in figures 2.5B, 2.6B and 2.7B and tabulated in Tables 2.2-2.3. Systematic bias of the TMS-1, in measuring steeper than keratometry for the steep meridian, was demonstrated (95% confidence limits -0.34 to -1.20 D). For the flat meridian power and corneal astigmatism measurements, no systematic bias was observed, however the range of the 95% confidence intervals is quite wide (0.66 to -1.10 D for the power of flat meridian; 0.51 to -1.45 D for astigmatism). Measurement disagreements as high as 9.6 D were recorded in the measurement of a given meridian on an individual patient basis. From Table 2.3 it can be seen that the difference in measurement of steep meridian power with the two instruments was within 0.25 D in 19.35% of the cases, and within 0.50 D in 45%; for the flat axis power the agreement was within 0.25 D in 26.6%, and within 0.50 D in 43% of the cases. Compared to the results obtained on normal corneas, the measuring disagreement was higher in the post-PKP eyes for all parameters [Tables 2.1, 2.2 and 2.3].

Location measurements

The measuring agreement of axis angle location in post-PKP corneas was found to be better ($12^{o} \pm 17^{o}$ for the steep meridian and $10^{o} \pm 16^{o}$ for the flat meridian location, Table 2.2) compared to the results obtained for normal corneas [Table 2.1], presumably because in highly astigmatic corneas identification of an astigmatic axis is easier than in corneas exhibiting very low degrees of astigmatism [Table 2.4].

TABLE 2.1 : Measuring agreement between keratometry and videokeratography on normal corneas (same observer)

Parameter measured	No eyes	Instrument	Power (D) (mean ± SD)	Mean difference (D) [km-TMS] ± SD	Limits of agreement (d ± 2SD)	95% confidence interval for bias*
Power of steep meridian	32	10 SL/O keratometer TMS-1	43.68 ± 1.29 44.36 ± 1.39	-0.68 (± 0.26)	-0.16 to -1.20 D	-0.58 to -0.78 D
Power of flat meridian	32	10 SL/O keratometer TMS-1	43.06 ± 1.24 43.48 ± 1.32	-0.41 (± 0.42)	0.43 to -1.25 D	-0.27 to -0.55 D
Astigmatism (D)	32	10 SL/O keratometer TMS-1	0.62 ± 0.36 0.88 ± 0.44	-0.26 (± 0.43)	0.60 to -1.12 D	-0.12 to -0.40 D
Location comparison			angle (°) (mean ± SD)	mean difference (°) [km-TMS] ± SD		
Steep meridian angle(°)	30	10 SL/O keratometer TMS-1	109° ± 37° 109° ± 44°	19° (± 19°) §	-19° to 57°	12° to 26°
Flat meridian angle (°)	30	10 SL/O keratometer TMS-1	166° ± 32° 157° ± 46°	17° (± 20°) §	-22° to 54°	10° to 24°

* bias is the mean difference [km-TMS], and 95% confidence limits calculated as d ± (t x SE), with t0.05, n-1 degrees of freedom
§ all values transformed to (+) difference in degrees
Angle degrees values have been rounded to absolute numbers

TABLE 2.2 : Measuring agreement between keratometry and videokeratography on astigmatic post-PKP corneas (same observer)

Parameter measured	No eyes	Instrument	Power (D) (mean ± SD)	Mean difference (D) [km-TMS] ± SD	Limits of agreement (d ± 2SD)	95% confidence interval for bias*
Power of steep meridian	31§	10 SL/O keratometer TMS-1	47.29 ± 3.01 48.06 ± 2.85	-0.77 (± 1.20)	1.63 to -3.17 D	-0.34 to -1.20 D
Power of flat meridian	30 ¥	10 SL/O keratometer TMS-1	41.72 ± 3.85 41.95 ± 3.12	-0.22 (± 2.35)	4.48 to -4.92 D	0.66 to -1.10 D
Astigmatism (D)	30 ¥	10 SL/O keratometer TMS-1	5.70 ± 3.15 6.16 ± 2.88	-0.47 (± 2.67)	4.87 to -5.84 D	0.51 to -1.45 D
Location comparison			angle (^{o}) (mean ± SD)	mean difference (^{o}) [km-TMS] ± SD		
Steep meridian angle(^{o})	30	10 SL/O keratometer TMS-1	$88^o \pm 54^o$ $91^o \pm 49^o$	12^o ($\pm 17^o$)	-19^o to 57^o	6^o to 18^o
Flat meridian angle (^{o})	30	10 SL/O keratometer TMS-1	$90^o \pm 54^o$ $94^o \pm 57^o$	10^o ($\pm 16^o$)	-22^o to 54^o	4^o to 16^o

* bias is the mean difference [km-TMS], and 95% confidence limits calculated as d ± (t x SE), with t0.05, n-1 degrees of freedom
§ 2/33 keratometric readings impossible ¥ in 3/33 eyes, keratometric mires very distorted, unreliable
Angle degrees values have been rounded to absolute numbers.

TABLE 2.3 : Distribution of difference in readings between 10 SL/O keratometer and TMS-1

	Normal corneas		Post-PKP corneas	
Difference between instruments (D)	Steep meridian	Flat meridian	Steep meridian	Flat meridian
0 - 0.25	2 (6.25%)	6 (18.75%)	6 (19.35%)	8 (26.6%)
0.25 - 0.50	8 (25%)	12 (37.5%)	8 (25.8%)	5 (16.6%)
0.50 - 1.00	16 (50%)	12 (37.5%)	12 (38.7%)	8 (26.6%)
1.00 - 1.50	6 (18.75%)	2 (6.25%)	3 (9.7%)	4 (13.3%)
1.50 - 3.00	-	-	-	1 (3.3%)
> 3.00	-	-	2 (6.4%)	4 (13.3%)
total	32 eyes	32 eyes	31 eyes	30 eyes

TABLE 2.4 : Distribution of differences in axis location obtained with the 10 SL/O keratometer and the TMS-1, compared to measured astigmatism, in normal corneas.

	Difference in axis measurement (degrees) between keratometer and TMS-1				
mean measured astigmatism (D)*	0 -10 degrees	10 - 20 degrees	20 - 30 degrees	> 30 degrees	
0 - 0.25	-	-	-	1 (3.3%)	steep meridian
	-	-	-	1 (3.3%)	flat meridian
0.25 - 0.50	1 (3.3%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	steep meridian
	1 (3.3%)	1 (3.3%)	2 (6.6%)	-	flat meridian
0.50 - 0.75	3 (10%)	3 (10%)	3 (10%)	2 (6.6%)	steep meridian
	3 (10%)	2 (6.6%)	4 (13.3%)	2 (6.6%)	flat meridian
0.75 - 1.00	-	2 (6.6%)	-	1 (3.3%)	steep meridian
	2 (6.6%)	1 (3.3%)	-	-	flat meridian
1.00 - 1.25	6 (20%)	2 (6.6%)	-	1 (3.3%)	steep meridian
	7 (23.3%)	2 (6.6%)	-	-	flat meridian
1.25 - 1.50	1 (3.3%)	1 (3.3%)	-	-	steep meridian
	1 (3.3%)	1 (3.3%)	-	-	flat meridian

* average by both instruments measurements
[Results on 30 paired measurements]

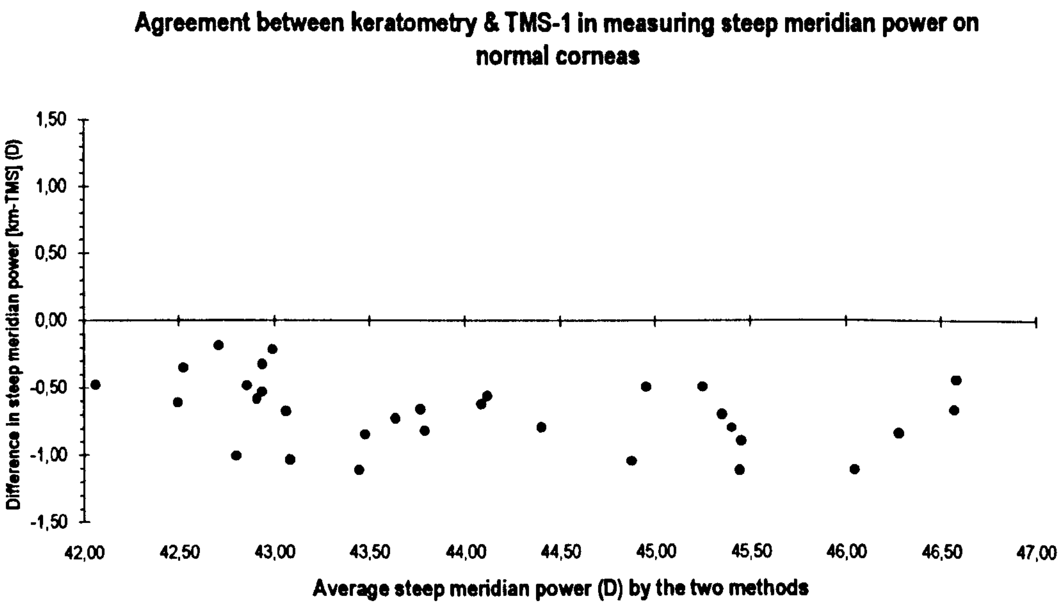


Figure 2.5 A

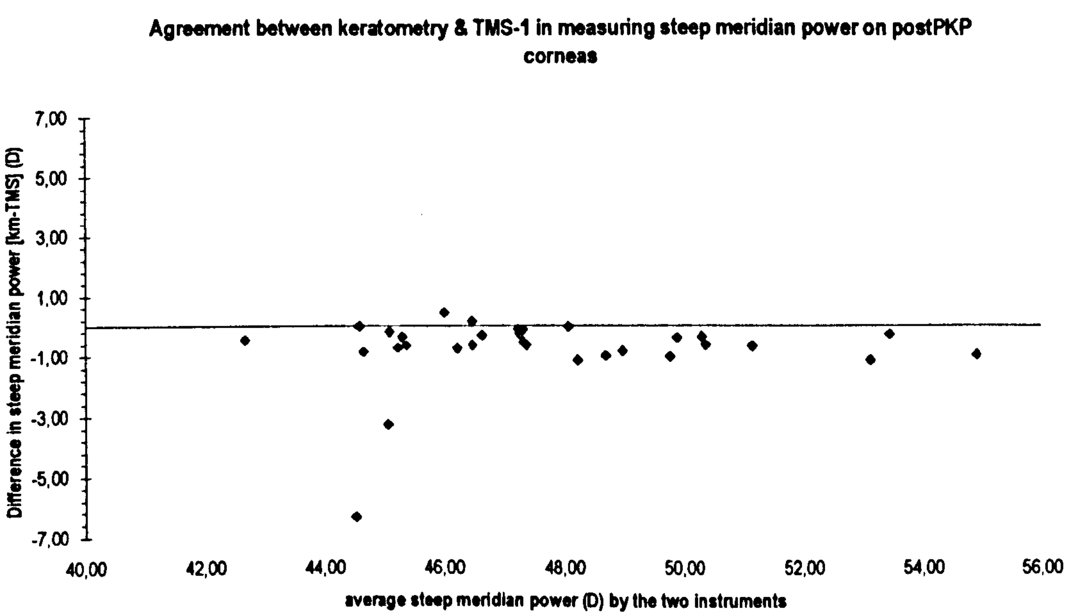


Figure 2.5 B

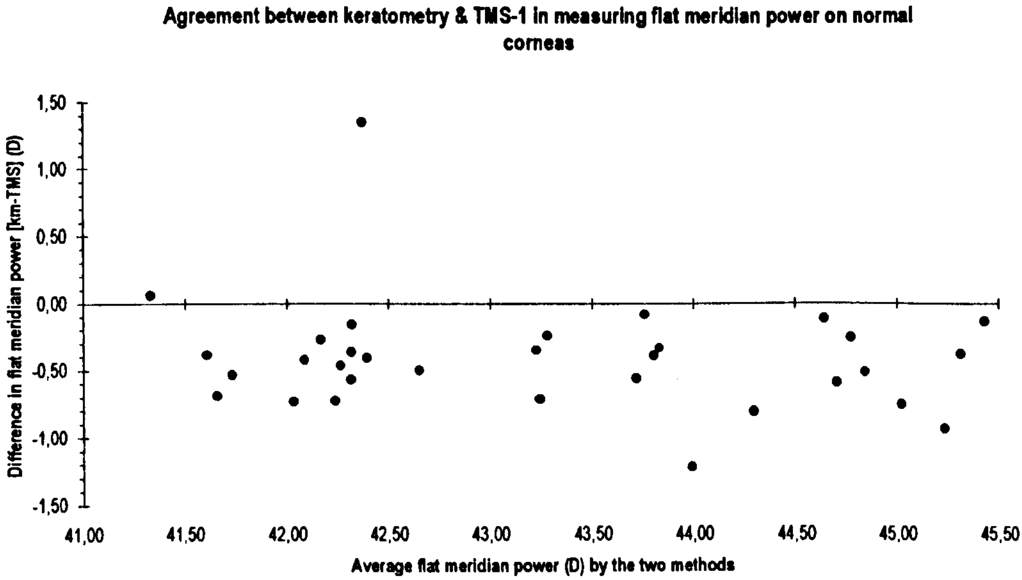


Figure 2.6 A

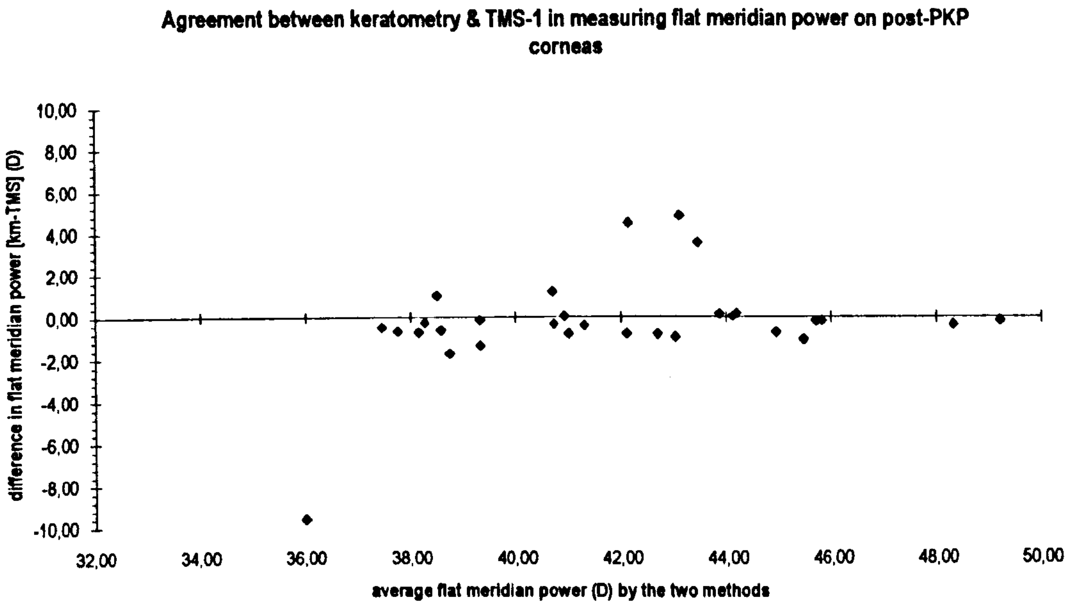


Figure 2.6 B

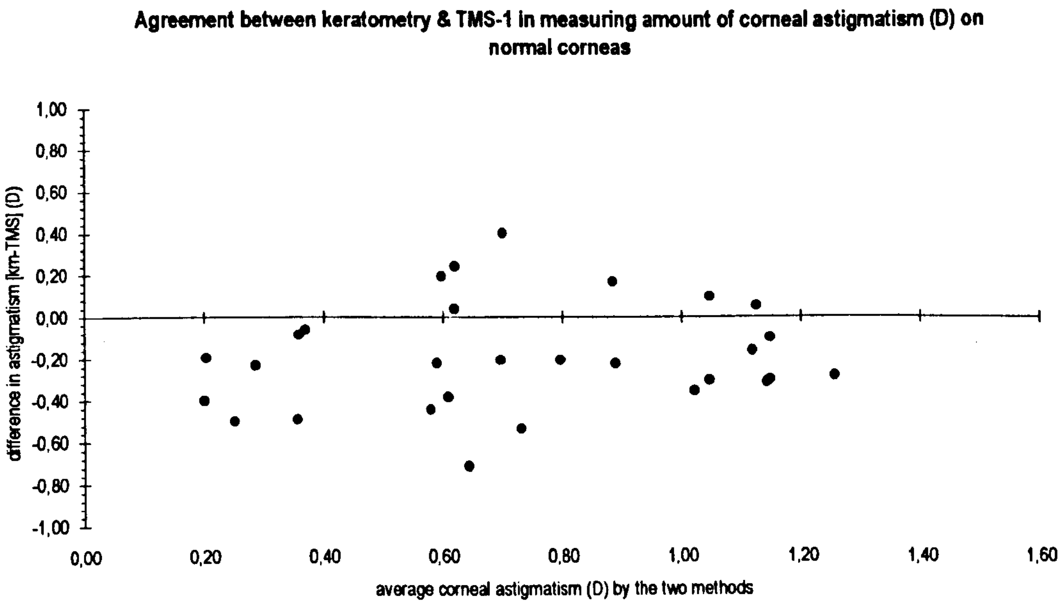


Figure 2.7 A

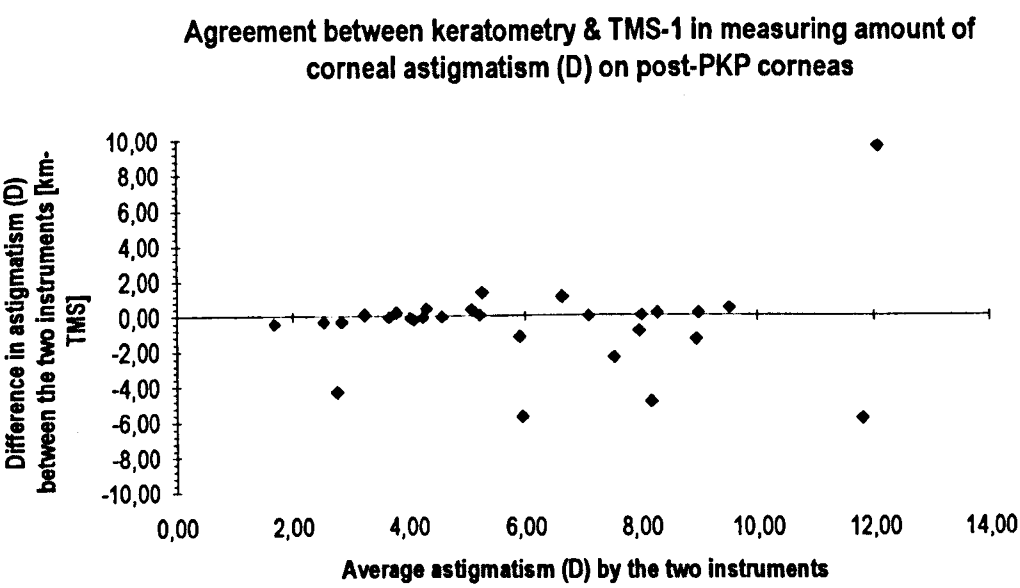


Figure 2.7 B

2.4.2. Intraobserver and interobserver variability

For the calculation of measuring agreement between the two instruments on normal as well as astigmatic corneas, the third series of measurements with each method, was selected. All the plot diagrams have been performed, although some of them may not be presented here.

2.4.2.-1. Repeatability of keratometer on normal corneas [Table 2.5]

The repeatability coefficients for all parameters measured were very comparable for both examiners 1 and 2. The mean variance (deviation score or mean difference) for steep and flat axes power, and astigmatism magnitude are zero or very close to zero for both examiners, although one of them (observer 1) was much more experienced than the other with the use of this particular keratometer model. The obtained intraobserver repeatability coefficients for steep axis power measurement (0.22 D and 0.18 D for observers 1 and 2 respectively), flat axis power (0.18 D and 0.16 D), astigmatism (0.26 D and 0.20 D), steep axis angle (5^{o} for both observers), and flat axis location (5^{o} and 8^{o}), are all considered at very acceptable level for clinical use of the instrument.

The inter-observer repeatability coefficients are slightly higher than the ones obtained with intraobserver measurements, but still within acceptable clinical levels [Table 2.5]. The inter-observer astigmatism repeatability coefficient was 0.28 D with only 4/66 measurements (6%) showing deviation score of more than 0.25 D from the mean value, and no measurements (0/66) with deviation more than 0.50 D.

2.4.2-2. Repeatability of TMS-1 on normal corneas [Table 2.6]

Significant differences were observed between the intraobserver coefficients of repeatability for the two observers. Observer 1 (experienced with the use of TMS-1), has shown consistently significantly lower coefficient values for all parameters except steep axis location, compared to observer 2 who was a novice user of the instrument. Although for observer 1 coefficients of repeatability reach clinically acceptable levels (0.30 D for steep axis power, 0.44 D for flat axis power, 0.40 D for astigmatism magnitude, 26° for steep axis location, 13° for flat axis location, 0.38 for SAI and 0.26 for SRI) these repeatability values are higher than those obtained when the same observer used the keratometer on the same study population [Table 2.5]. For the novice observer 2, the obtained coefficients of repeatability are above of what can be considered clinically acceptable in measuring steep axis power (1.08 D), flat axis power (1.96 D), astigmatism magnitude (1.62 D), SAI (0.90) and SRI (0.54). The repeatability for axes location is clinically acceptable for the steep axis (22°) but not for the flat (30°). These results highlight the superior repeatability performance of the keratometer compared to videokeratography, as well as the greater implication that user's experience has on the reproducibility of TMS-1 compared to the keratometer. For the astigmatism measurement, observer 1 had 4/33 measurements (12%) with deviation score > 0.25 D, but in only one of these measurements the deviation was at the range between 0.50 D and 1.00 D [Figure 2.8A]. For observer 2, there were 5/33 measurements (15%) with deviation score > 0.25 D, but for 3 of these 5 measurements the deviation was more than 1.00 D [Figure 2.8B]. It is also obvious from the plot diagram that the high deviation scores were observed for corneas with higher astigmatism.

As it might be expected, the higher variability in observer's 2 readings, affects the inter-observer variability as well [Table 2.6]. All parameter's coefficients are outside the clinical acceptable limits. This is particularly so, for the measurement of flat axis power (1.82 D), and axes location (40° for the steep axis, 42° for the flat axis).

2.4.2-3. Repeatability of keratometer on post-PKP corneas [Table 2.7]

Both observers (equally experienced with the use of keratometer)* have shown significantly wide repeatability coefficients for all parameters apart from axes location [Table 2.7]. For observer 1, mean of differences, SD of differences and

* although refered again as observers 1 and 2, are not the same as observers 1 and 2 of the studies on normal corneas. However, observer 1 is the same for both studies.

coefficients of repeatability for all measured parameters are significantly higher than those observed on the normal corneas population study [Table 2.5]. This indicates that the repeatability of the keratometer decreases when studying highly astigmatic corneas. For observer 2, coefficient of variability and SD are even greater than observer 1 [Table 2.7]. However, observer 2 showed a better performance than observer 1 in identifying the axis location. Figures 2.9A and 2.9B show the plot diagrams for the repeatability in astigmatism measurements for examiners 1 and 2 respectively.

Results on inter-observer repeatability of the keratometer on post-PKP corneas are also shown on Table 2.7; the interobserver astigmatism measurement repeatability is represented graphically in Figure 2.9C.

2.4.2.-4. Repeatability of TMS-1 on post-PKP corneas [Table 2.8]

Both observers 1 and 2 (both very experienced with the TMS-1 use), demonstrated poor repeatability in the highly astigmatic group. The poor performance is highlighted by the high values of mean variance, SD and repeatability coefficients for both examiners in the measurement of steep axis power, flat axis power, astigmatism magnitude, flat axis angle and SRI [Table 2.8]. Steep axis location and SAI were the only measurements that showed a variability measurement acceptable for clinical purposes. Compared to keratometer [Table 2.7], the TMS-1 demonstrated a much higher range of variability in measuring post-PKP corneas. The worse repeatability of the TMS-1 on post-PKP corneas than on normal corneas, is directly evident by the measurements of the same observer 1 on normal corneas [Table 2.6] and post-PKP corneas [Table 2.8]. Intra- and inter-observer variability of TMS-1 on measuring astigmatism on post-PKP corneas is shown on figures 2.10A to 2.10C.

TABLE 2.5 : Repeatability of 10 SL/O Zeiss keratometer on normal corneas

	Observer 1		Observer 2		Observers 1 and 2	
	variance mean ± SD	intraobserver coefficent of repeatability	variance mean ± SD	intraobserver coefficent of repeatability	variance mean ± SD	inter-observer coefficent of repeatability
Steep axis power (D)	0.02 ± 0.11	0.22 D	0 ± 0.09	0.18 D	0* ± 0.12	0.24 D
Flat axis power (D)	0.01 ± 0.09	0.18 D	0* ± 0.08	0.16 D	0.009 ± 0.10	0.20 D
Astigmatism (D)	0.01 ± 0.13	0.26 D	0.002 ± 0.10	0.20 D	0.00 ± 0.14	0.28 D
Steep axis angle	$3^o \pm 3^o$	5^o	$3^o \pm 3^o$	5^o	$4^o \pm 4^o$	8^o
Flat axis angle	$3^o \pm 3^o$	5^o	$3^o \pm 4^o$	8^o	$5^o \pm 4^o$	8^o

* value very close to 0.
Coefficient of repeatability calculated as 2 x SD
Angle degrees values have been rounded to absolute numbers.

TABLE 2.6 : Repeatability of the TMS-1 videokeratoscopy system on normal corneas

	Observer 1		Observer 2		Observers 1 and 2	
	variance mean ± SD	intraobserver coefficent of repeatability §	variance mean ± SD	intraobserver coefficent of repeatability §	variance mean ± SD	inter-observer coefficent of repeatability §
Steep axis power (D)	0.07 ± 0.15	0.30 D	-0.05 ± 0.54	1.08 D	0.009 ± 0.46	0.92 D
Flat axis power (D)	-0.08 ± 0.22	0.44 D	-0.26 ± 0.98	1.96 D	-0.17 ± 0.91	1.82 D
Astigmatism (D)	0.00 ± 0.20	0.40 D	-0.20 ± 0.81	1.62 D	-0.10 ± 0.63	1.26 D
Steep axis angle	$8^o \pm 13^o$	26^o	$11^o \pm 11^o$	22^o	$15^o \pm 20^o$	40^o
Flat axis angle	$7^o \pm 7^o$	13^o	$7^o \pm 15^o$	30^o	$14^o \pm 21^o$	42^o
SAI	0.004 ± 0.19	0.38	-0.001 ± 0.45	0.90	0 ± 0.39	0.78
SRI	0.003 ± 0.13	0.26	-0.016 ± 0.27	0.54	0.01 ± 0.27	0.54

§ Coefficient of repeatability calculated as 2 x SD
Angle degrees values have been rounded to absolute numbers.

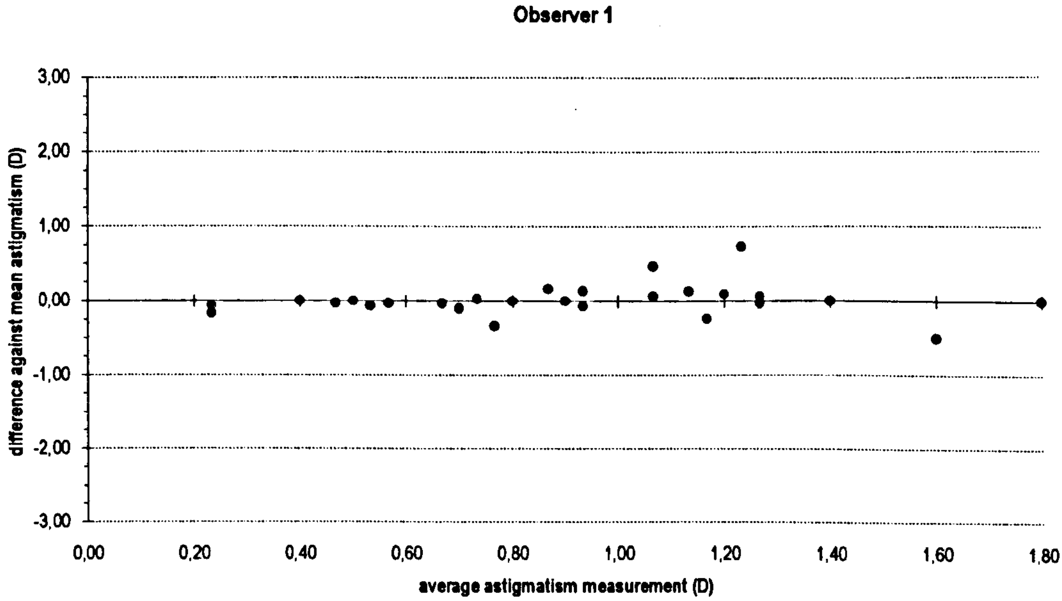


Figure 2.8 A Observer 1 variation in measuring astigmatism magnitude (D) with the TMS-1 on normal corneas

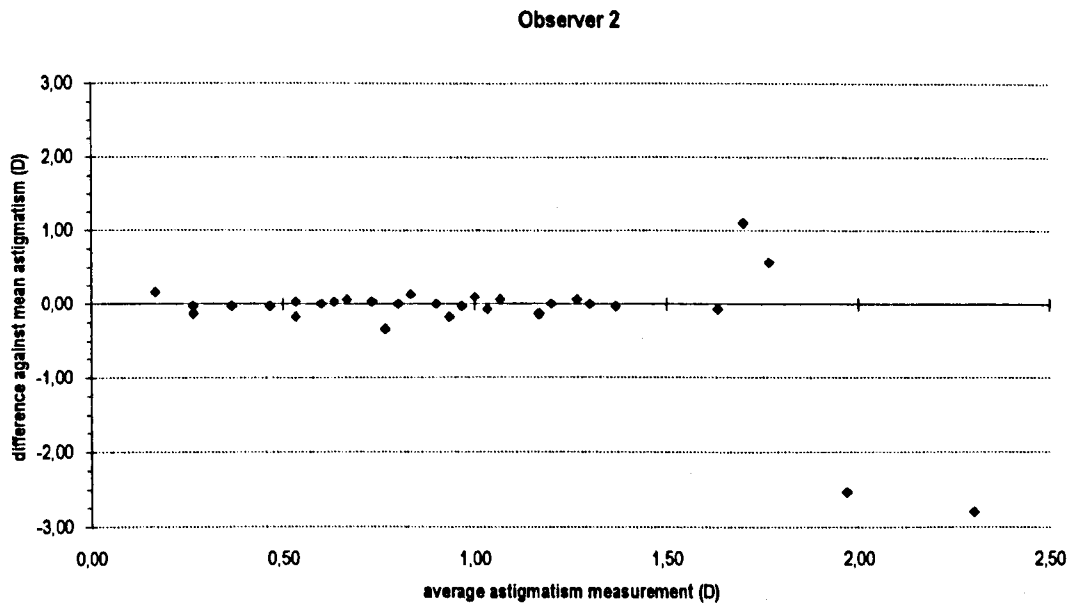
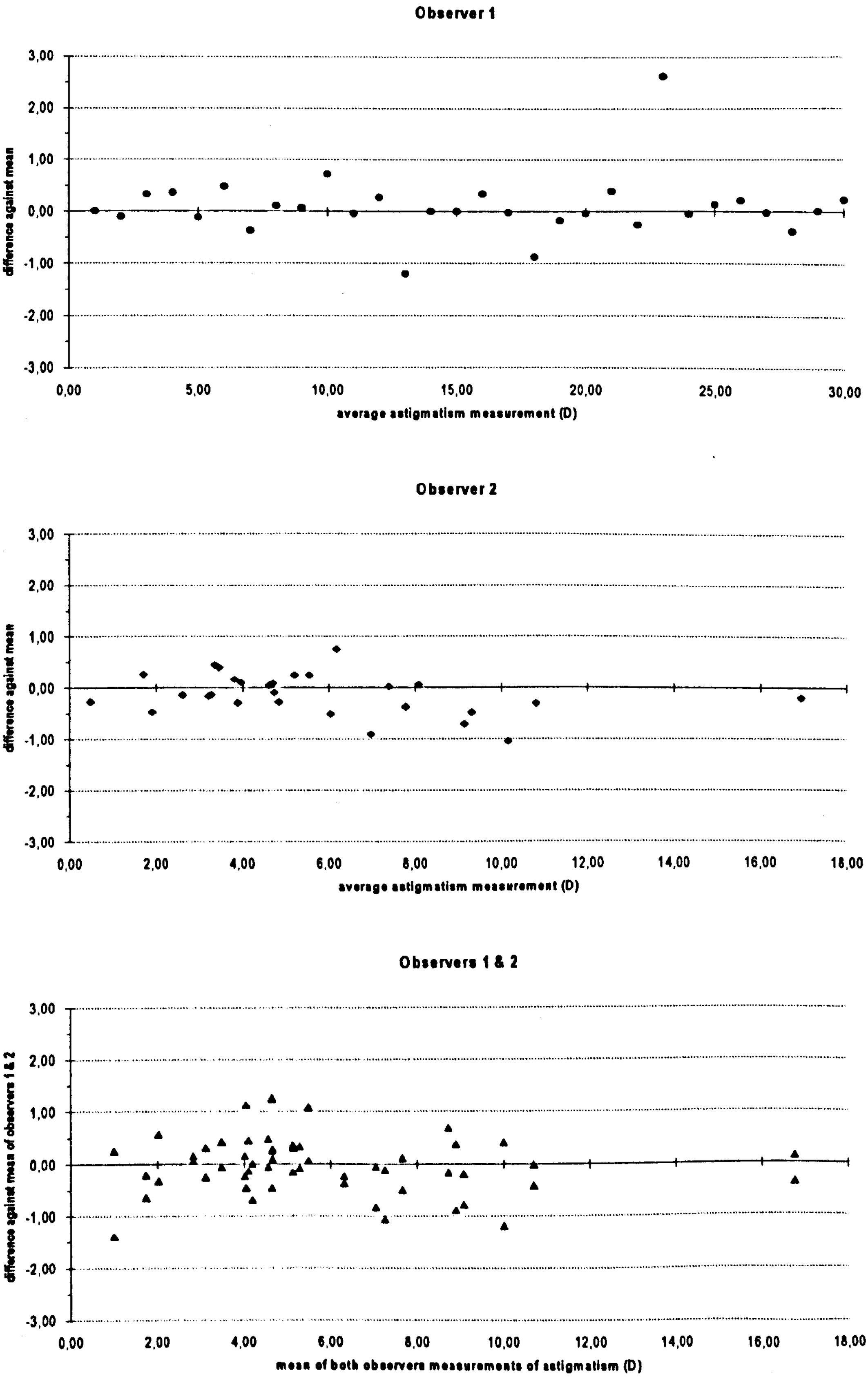


Figure 2.8 B Observer 2 variation in measuring astigmatism magnitude (D) with the TMS-1 on normal corneas

TABLE 2.7 : Repeatability of 10 SL/O Zeiss keratometer on post-PKP corneas

	Observer 1		Observer 2		Observers 1 and 2	
	variance mean ± SD	intraobserver coefficent of repeatability	variance mean ± SD	intraobserver coefficent of repeatability	variance mean ± SD	inter-observer coefficent of repeatability
Steep axis power (D)	-0.05 ± 0.44	0.88 D	-0.13 ± 0.47	0.94 D	-0.06 ± 0.52	1.04 D
Flat axis power (D)	-0.11 ± 0.66	1.32 D	0.04 ± 0.40	0.80 D	-0.04 ± 0.51	1.02 D
Astigmatism (D)	0.09 ± 0.62	1.24 D	-0.13 ± 0.41	0.82 D	-0.02 ± 0.56	1.12 D
Steep axis angle	$2^{o} \pm 2^{o}$	5^{o}	$4^{o} \pm 9^{o}$	18^{o}	$4^{o} \pm 5^{o}$	10^{o}
Flat axis angle	$3^{o} \pm 4^{o}$	8^{o}	$5^{o} \pm 10^{o}$	20^{o}	$5^{o} \pm 6^{o}$	12^{o}

Coefficients of repeatability calculated as 2 x SD
Angle degrees values have been rounded to absolute numbers.

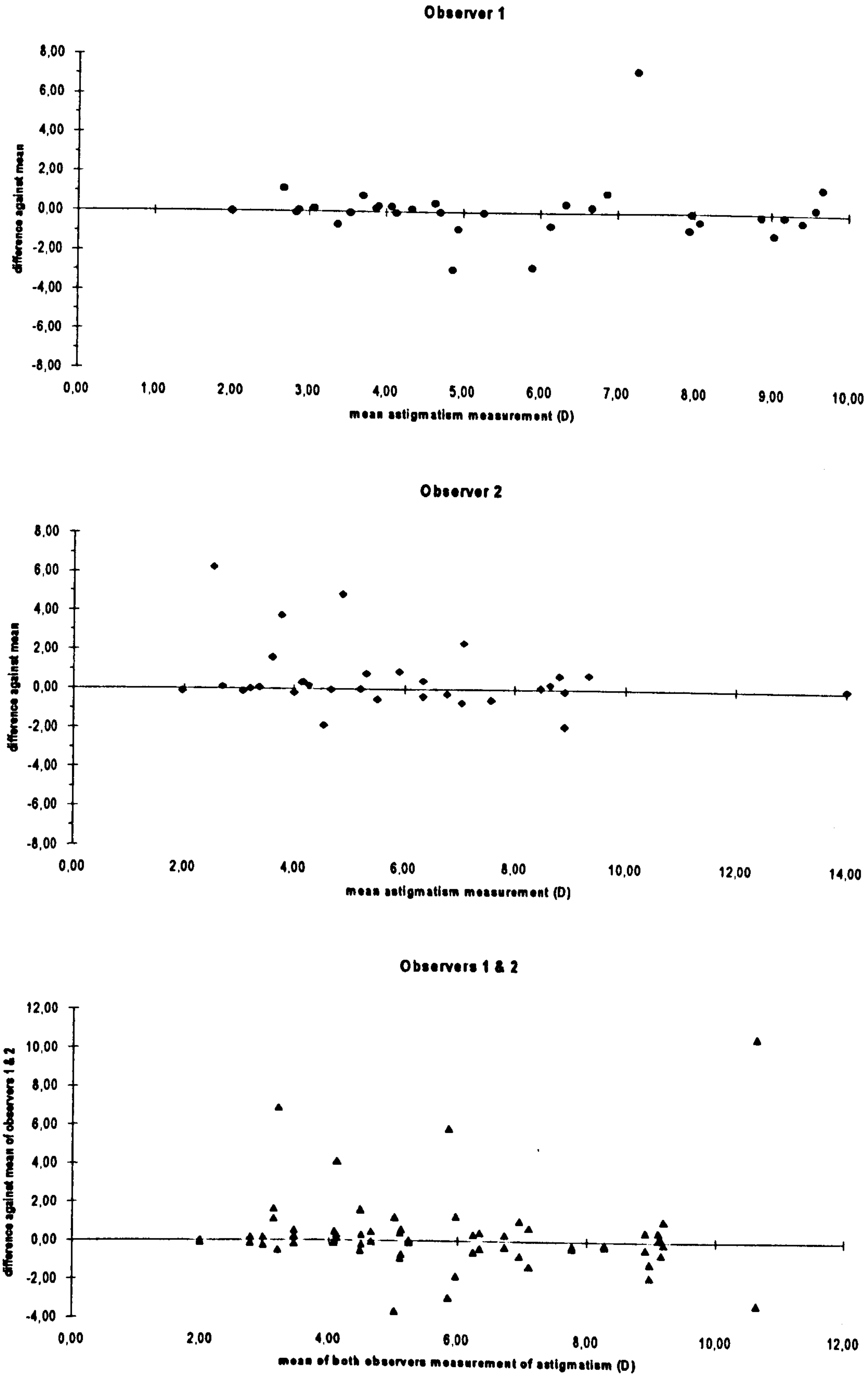


Figures 2.9 : Repeatability of keratometer on post-PKP corneas **A(top)**:for observer 1, **B(middle)**:for observer 2, **C(bottom)**:for both observers 1 and 2.

TABLE 2.8 : Repeatability of the TMS-1 videokeratoscopy system on post-PKP corneas

	Observer 1		Observer 2		Observers 1 and 2	
	variance mean ± SD	intraobserver coefficent of repeatability §	variance mean ± SD	intraobserver coefficent of repeatability §	variance mean ± SD	inter-observer coefficent of repeatability §
Steep axis power (D)	0.09 ± 0.71	1.42 D	0.015 ± 0.91	1.82 D	0.05 ± 0.94	1.88 D
Flat axis power (D)	0.36 ± 1.38	2.76 D	-0.07 ± 1.89	3.78 D	0.15 ± 1.93	3.86 D
Astigmatism (D)	0.52 ± 1.65	3.30 D	0.08 ± 1.56	3.12 D	0.30 ± 2.03	4.06 D
Steep axis angle	$5^{o} \pm 6^{o}$	12^{o}	$4^{o} \pm 6^{o}$	12^{o}	$9^{o} \pm 17^{o}$	34^{o}
Flat axis angle	$12^{o} \pm 15^{o}$	30^{o}	$10^{o} \pm 18^{o}$	36^{o}	$13^{o} \pm 17^{o}$	34^{o}
SAI	0.05 ± 0.19	0.38	0.02 ± 0.15	0.30	0.03 ± 0.18	0.36
SRI	0.09 ± 0.51	1.02	0.06 ± 0.24	0.48	0.08 ± 0.45	0.90

§ Coefficient of repeatability calculated as 2 x SD
Angle degrees values have been rounded to absolute numbers.



Figures 2.10 : Repeatability of TMS-1 on post-PKP corneas. A(top): for observer 1; B(middle): for observer 2; C(bottom): for both observers 1 and 2.

2.5. Discussion

As new methods for corneal curvature measurement have been introduced in everyday clinical practice, the users of the CAVK devices need to know the practical limitations of these instruments and how they compare to less sophisticated ones such as the keratometer. A new method has to be evaluated by comparison to an established technique especially where no "gold standard" is available.

The ophthalmic literature on the comparison of methods of measurement of the corneal contour, is extremely variable in terms of clinical and statistical methods used for the analysis of the validity and repeatability of the various instruments. Some investigators compared instruments or inter and intraobserver variability using inappropriate statistical methods such as correlation analysis (*Davis & Dresner,* 1991; *Wilson et al,* 1992a) while other studies look only on the accuracy and precision of the instruments on test surfaces (*Hannush et al,* 1989; *Legeais et al,* 1993; *Antalis et al,* 1993; *Maguire et al,* 1993).

In the present study, the degree of agreement between keratometry and video-keratography as well as inter and intraobserver variability was assessed by avoiding the use of a correlation coefficient, as this is reported consistently in the medical statistical literature as misleading and inappropriate for comparison of methods (*Altman et al,* 1983; *Bland & Altman,* 1986; *Shaw et al,* 1994). A high correlation does not necessarily mean that the two methods agree, as data which seem to be in poor agreement can produce quite high correlations. On the other hand even with significant bias, the differences between two methods may be clinically small enough for the methods to be used interchangeably (*Shaw et al,* 1994). In this study a previously described analysis technique for method comparison data (*Bland & Altman,* 1986) was employed instead.

Previous studies have assessed the accuracy and precision of the instruments on measuring artificial surfaces, but it is not that an instrument capable of accurate readings on test spheres can be equally accurate on aspherical surfaces such as the human cornea. Furthermore, in the case of normal and astigmatic corneas, the absolute power is unknown and it is therefore impossible to measure the accuracy in these cases. Instead, the reproducibility (= precision, repeatability) of the instrument can be assessed.

Hannush et al. (1989), comparing keratometer to CMS on steel spheres, found measurements to be within ±0.27 D of the calibrated value for both instruments, concluding that both show an accuracy within the clinically acceptable range. However, the CMS measurements were found to be less accurate for surfaces steeper than the normal corneas (50 D test ball). *Legeais et al.* (1993) evaluated the accuracy of a vertically mounted TMS-1 system. The assessment was performed on six calibrated PMMA spheres by two examiners. It was found that the accuracy of the 25 rings decreased from the centre to the periphery, and the deviation scores were within ±0.25 D only for the 43 D sphere. The accuracy decreased progressively with flatter or steeper spheres. Comparison studies of accuracy between different models of videokeratography on calibrated spheres, have also been performed by other investigators, with inconsistent results. *Wilson et al.* (1992a) comparing the TMS-1 to the EyeSys model, found the TMS-1 to be more accurate for measurements at the apex or 1 mm from the apex, whereas the EyeSys measurements were more accurate at 3 mm from the apex, for calibrated spheres of different radius of curvature. In contrast to these findings, *McCarey et al.* (1992) found the data from the 3 mm chord circle on calibrated spheres, to be the least accurate for the EyeSys instrument. The 3 mm zone for the 55.35 D target showed a reproducibility of 0.32 D (beyond the expected accuracy of 0.25 D). *Maguire et al.* (1993), who also evaluated the reproducibility of the TMS-1 and EyeSys systems on test spheres, found significant greater variability of readings for the EyeSys system for readings obtained within 0.60 mm of the vertex normal for all three test spheres. The TMS-1 system instead, showed equally consistent readings within 0.60 mm as well as between 0.61 and 1.5 mm from the vertex normal.

In the study presented here, first the measurement agreement between the keratometer (Zeiss model 10 SL/0) and videokeratography (TMS-1 model) on normal corneas was evaluated. Statistically significant differences were found between the two instruments in measuring both steep and flat meridians as well as corneal astigmatism. There was a systematic bias of the TMS-1 to measure steeper than the keratometer, for both principal meridians on a consistent basis. This finding is in agreement with *Hannush et al.* (1989) who found that the keratometer (Bausch & Lomb) generally read lower values, and the CMS higher values than calibrated steel spheres. This difference was noted with both investigators used in the study and for the steel balls of all four different dioptric values (38 D, 42 D, 43 D and 50 D). Although the authors reported the differences not to be statistically significant, they came to that conclusion by only comparing the mean deviation scores (mixed-model ANOVA). In that study, the mean difference between the two instruments was between 0.18 to 0.22 D (for the two observers). In another study on 20 normal corneas, *Koch et al.* (1989) found the mean absolute difference between the keratometer (Macro model I) and the EyeSys device to be 0.19 D for the steep meridian power and 0.21 D for the flat meridian. In their study as well, higher mean values were given by the EyeSys than by the keratometer for both steep and flat meridian power. In our study, the differences between the two instruments were higher (0.68 D, SD 0.26 for the steep meridian, and 0.41 D, SD 0.42 D for the flat meridian). *Davis & Dresner* (1991), performed their own comparison study between the keratometer (Marco model-1) and the EH-270 corneal topography system. For readings obtained from 14 normal corneas, excellent correlation was achieved between keratometry and the EH-270 (0.969 for the vertical meridian and 0.972 for the horizontal meridian measurements). Although the results of that study cannot be directly compared to the present one because of the different statistical methods used, a re-analysis of *Davis & Dresner* data (original paper's table 2) shows that also the EH-270 device produces slightly steeper readings than the keratometer (0.01 D for the horizontal meridian and 0.13 D for the vertical meridian).

In another study *Tsilimbaris et al.* (1991) have found a statistically significantly steeper average value (0.13 ± 0.47 D) given from the EyeSys unit compared to keratometry for the flat (vertical) meridian in 92 normal eyes. However, no statistically significant difference was found for the steep meridian power (-0.06 ± 0.61 D). A mean negative bias has also been observed of the Alcon portable automated keratometer versus TMS-1, of 0.25 to 0.40 D with statistical significance in approximately 50% of the measurements (*Palmer & Reid,* 1994). The bias was observed in measurements of both steep and flat meridians, but it was more apparent for the flat meridian.

Zadnik et al. (1995) have found results very similar to the results of the present study, by comparing keratometry (Bausch & Lomb) to TMS-1 on 29 normal eyes, and by using the same statistical procedures as in this study. TMS-1 videokeratography yielded significantly steeper corneal curvature values when compared to keratometer, in both the horizontal (mean -0.47 D, SD 0.47 D) and the vertical meridians (mean -0.22, SD 0.57 D).

There is therefore quite strong evidence from a number of previous studies indicating an inherent tendency of the CAVK devices to measure more steep than the keratometer. This is not a fact related to a specific model, but rather shared by instruments of different manufactures (TMS-1, EyeSys, EH-270). This was also a very consistent finding of the present study. Some differences seen with the results of previous studies, may be contributed to one of several factors such as the use of different keratometry and CAVK models, the use of different test surfaces (calibrated spheres, normal corneas), or the use of different statistical methods in the various studies [Table 2.9].

TABLE 2.9 : Previous studies on measuring agreement between keratometry and videokeratoscopy on spherical and aspherical surfaces

Study	Instruments tested	Tested on....	No observers	Measuring agreement	Statistical test
Hannuch et al,1989	Keratometer (B & L) Corneascope, CMS	Calibrated steel spheres	2 (x3)	No significant difference between the 3 instruments (p >.05)	Hartley test
Koch et al, 1989	Keratometer, EyeSys	20 normal corneas	3 (x3)	mean difference 0.19 D for steep meridian power, 0.21 D for flat meridian power	
Tsilimbaris et al, 1991	EyeSys, Javal keratometer	92 normal eyes	1	Significant differences in mean flat meridian power, mean astigmatism and steep meridian location. Clinically meaningful difference seen only in eyes with km astigmatism >1.5 D	paired t-test, Wilcoxon for location of meridians
Davis & Dresner, 1991	keratometer, EH-270	14 normal eyes	1 (x5)	very good correlation for both horizontal and vertical meridians	correlation coefficient
Wilson et al, 1992a	TMS-1, EyeSys vs Keratometry	22 normal corneas	1	Statistically significant difference in astigmatism between km/ EyeSys; not statistical difference between km/TMS	correlation coef. & non-parametric Wilcoxon
Palmer & Reid, 1994	autokeratometer, TMS-1	23 normal corneas	2 (x3)	negative bias of autokeratometer vs TMS-1 of 0.25-0.40D with statistical significance in 50%	correlation coefficient
Zadnik et al, 1995	keratometer, photo-keratography, TMS-1	29 normal eyes	1 (x3)	-0.47 ± 0.47 D for horizontal meridian power -0.22 ± 0.57 D for vertical meridian power	Altman & Bland method
McCarey, 1992	EyeSys, keratometer	toric PMMA CLs of known curvature	?one	both keratometry and EyeSys underestimated the expected cylinder	-
Antalis et al, 1993	TMS-1 & EyeSys vs keratometry	11 'abnormal' corneas of various diagnoses	1	Correlation: TMS vs EyeSys : .9901 for flat k, .9937 for steep k, .9806 for axis. CAVK vs km correlation : .9617 to .9844	correlation coefficient, paired t-test, ANOVA

The results of the present study were significantly different for steep and flat meridian power measurement. Although a tendency of the TMS-1 to record higher astigmatism than the keratometer was observed, the results of astigmatism magnitude and meridian locations were similar between the two instruments and approached clinically acceptable agreement.

Tsilimbaris et al. (1991) in their study, found a clinically significant difference (0.84 ± 0.64 D) between the EyeSys and Javal keratometer when measuring astigmatic eyes with cylinder greater than 1.50 D, but only 18 of the 92 eyes of their study fell into this category. This is a finding that is supported by the results of the present study on post-PKP corneas where a difference of 0.47 ± 2.67 D was observed on highly astigmatic corneas.

Wilson et al. (1992a) checked on the agreement between keratometry (Bausch & Lomb), TMS-1 and EyeSys on 22 normal corneas. They found that in measuring corneal astigmatism, there was statistically significant difference between keratometer and EyeSys (with EyeSys underestimating the keratometer cylinder by about 23%); the difference between keratometer and TMS-1 however, was not significant. It was also found that the mean difference in locating major cylinder axis between TMS-1 and keratometer was 21.3 ± 28.1°, and that the TMS-1 had more difficulty in identifying the major corneal axis in corneas with lower cylinders. The latter results are in agreement with the findings of the present study (19° ± 19° for the steep meridian, 17° ± 20° for the flat, better location agreement in higher cylinders, Table 2.3).

In evaluating agreement on astigmatic post-PKP corneas, again a bias of the TMS-1 in measuring higher power of the steep meridian, higher power of the flat meridian, and higher magnitude of astigmatism than the keratometer was observed. This bias was not as strong as for the normal corneas (apart from the power of steep meridian). However the limits of agreement (mean ± 2SD) between the two instruments can be considered unacceptable for clinical purposes.

It was observed that these limits of measuring agreement were 1.63 to -3.17 D for steep meridian power, 4.48 to -4.92 D for flat meridian power, and 4.87 to -5.84 D for the astigmatism magnitude. This means that the two instruments cannot be used interchangeably in comparing results of highly astigmatic post-PKP corneas. In terms of meridian angle location with the two instruments on post-PKP corneas, they were found to be very close together with agreement better than that obtained for normal corneas. Presumably this is because identification of meridians is easier in astigmatic than non astigmatic corneas. However, it must be pointed that in a significant number of examinations of the flat meridians (4/33, 12%) very distorted keratometric mires were seen, making measurements impossible, whereas in 2/33 examinations (6%), the TMS-1 recorded (incorrectly) a "spherical" cornea. Corneal transplantation tends to steepen keratometric readings, decreasing keratometer mire image size. The mean (± SD) of keratometric readings for the steep meridian of post-PKP corneas was 47.29 ± 3.01 D [Table 2.2], whereas the same readings for the normal corneas were 43.68 ± 1.29 D [Table 2.1]. The astigmatism measurements were 0.62 ± 0.36 D with keratometry, 0.88 ± 0.44 D with TMS-1 for the normal corneas [Table 2.1]. For the post-PKP corneas astigmatism measured with keratometer was 5.70 ± 3.15 D, and with TMS-1 6.16 ± 2.88 D [Table 2.2]. Because keratoplasty produces high and irregular astigmatism (especially within the first year), this explains that the SD of measurements was much greater in this group of eyes compared to normal eyes.

No similar studies are available in the literature comparing directly the performance of keratometer and CAVK on highly astigmatic, irregular corneas. However, the results of this study, can be supported by findings of previous studies on test surfaces. *Hannush et al.* (1989), found CMS measurements to be less accurate for surfaces steeper than normal corneas (50 D test ball). *McCarey et al.* (1992) found the EyeSys less reproducible for the 55.35 D target, with reproducibility being 0.32 D (beyond the expected accuracy of 0.25 D). *McCarey* *et al.* (1992) measuring two aspheric PMMA contact lenses of known curvature, found that the keratometer and the EyeSys unit provided a close approximation of the surface characteristics of the lenses, but also found that both instruments underestimated the expected cylinders. The latter result must be seen with the criticism that different refractive indices were used for the calculations of the refractive powers when using the instruments (1.3375) or the contact lenses (1.490). *Legeais et al.* (1993), also reported that the accuracy of TMS-1 reduced with flatter or steeper spheres. In a clinical study of 18 abnormal corneas with a variety of conditions (keratoconus, corneal scars, residual postoperative astigmatism following refractive surgery), *Antalis et al.* (1993) compared the EyeSys and the TMS-1 in terms of central radius of curvature. The average differences for the two instruments were -0.2 ± 0.7 D for the flat meridian, -0.7 ± 0.9 D for the steep meridian, and 3 ± 11° for the steep axis. Neither system worked ideally for severely irregular corneas. Correlations for the two instruments were 0.9901 and 0.9937 for the flat and steep meridians respectively. Both instruments were also found to correlate relatively well, although less, with the keratometer (r = 0.9617 to 0.9844). The paper however suffers the deficiency of using correlation coefficients to compare the agreement of instruments, and the small number of eyes compared (14 of the original 18, as in 4 patients the readings were too irregular to be measured).

The intra- and interobserver repeatability results on normal corneas, have shown that the keratometer reproducibility is excellent for all measured parameters, at very acceptable clinical levels and independent of the observer's level of experience with the instrument. Compared to the TMS-1, keratometer has shown a superior repeatability in normal corneas (intraobserver coefficients of repeatability for keratometry and TMS-1 respectively : 0.22 and 0.30 D for steep meridian power, 0.18 and 0.44 D for flat meridian power, 0.26 and 0.40 D for astigmatism, 5° and 26° for steep meridian location, 5° and 13° for flat meridian location).

An account of previously performed studies on reproducibility of keratometry and CAVK can be seen on Table 2.10. *Hannush et al.* (1989), although measuring steel balls found no significant difference in terms of reproducibility between keratometry and videokeratoscopy (CMS), another study on 18 normal corneas (*Hannush et al,* 1990) concluded that the keratometer was more reproducible than the CMS and the Corneascope. For a deviation less than 0.25 D, it was estimated that the CMS is 83% as reproducible as a keratometer reading at the edge of the 3-mm central zone on normal human corneas. For the CMS, rings 2 to 13 were reasonably reproducible (< 0.5 D difference) in 76% of the examined cases. These results indicate that studies on test surfaces and human corneas may produce different results that should be interpreted accordingly. *Legeais et al.* (1993), have also found that the SK-1 autokeratometer was more reproducible (SD < 0.10 D) than a vertically mounted TMS-1 (SD ≤ 0.30 D), on testing calibrated spheres. By using the same statistical tests as in the current study, *Zadnik et al.* (1995) have found the interoccasion repeatability (one examiner) of the keratometer to be with 95% of confidence limits of -0.52 to 0.46 D for the horizontal meridian and -0.74 to 0.55 D for the vertical meridian. In our study the 95% confidence limits for the keratometer were 0.07 to 0.15 for the steep meridian power, and 0.07 to 0.11 for the flat meridian power (observer 1), results that compare very favourably to the above. On the other hand TMS-1 repeatability was found in our study to be observer related. The novice observer 2, demonstrated much bigger variability on his measurements compared to the experienced examiner 1 [Table 2.6]. No such difference between the two observers was noticed for the keratometer. On the other hand, observers of similar experience produced similar results with the TMS-1, on post-PKP corneas. Intraobserver variation with the TMS-1 was also found to be astigmatism related, and increases with increasing astigmatism. In the study conducted by *Hannush et al.* (1990), a significant difference in the repeatability of the CAVK measurements between the two investigators was found and it was concluded that the examiner's technique plays a role in the

TABLE 2.10 : Previous studies comparing reproducibility of keratometry and videokeratoscopy

Study	Instruments tested	Tested on....	No observers	Reproducibility (= precision, repeatability)	Statistical test
Hannush et al,1990	Keratometer (B & L) Corneascope, CMS	18 normal corneas	2 (x3)	Keratometer more reproducible than CMS (83% as reproducible)	Hartley test
Davis & Dresner, 1991	EH-270, keratometer	14 normal eyes	1 (x5)	For steeper corneas, EH-270 less reproducible than keratometer	t-test
Koch et al, 1992	EyeSys, keratometer	20 normal corneas, steel and PMMA spheres	3	for spheres: reproducibility for both instruments < 0.12 D for normal corneas: keratometer reproducibility slightly better than EyeSys	
Legeais et al, 1993	vertically mounted TMS, autokeratometer	calibrated spheres	2 (x3)	SK-1 more reproducible (SD <0.10 D) than TMS (SD < 0.30 D)	Hartley test
Maguire et al, 1993	TMS-1 vs EyeSys	test spheres	1 (x4)	greater variability for EyeSys than TMS, for readings within 0.6 mm of the vertex normal	Duncan's multiple comparison
Zadnik et al, 1995	TMS-1, keratometer, photokeratoscope	29 normal eyes	1 (x3)	Reproducibility of TMS worse moving from centre to periphery	95% CI

measurements. The suggestion that for the TMS-1, operator reliability improves with training was also reported in a poster presentation by *Patel et al.* (1994) who tested the inter-observer reliabilities of three corneal topographers (TMS, EyeSys, Euclid topographer). Other investigators (*Legeais et al,* 1993) have found no statistical difference between investigators.

The present study also revealed that on measuring highly astigmatic post-PKP corneas, the keratometer becomes less repeatable than on normal corneas (compare Tables 2.5 to 2.7). However, compared to the TMS-1, the keratometer achieved a much superior reproducibility (Table 2.7 vs Table 2.8). The repeatability of TMS on post-PKP corneas was poor (interobserver coefficients of repeatability were 1.88 D for steep meridian power, 3.86 D for flat meridian power, 4.06 D for astigmatism, 34^{o} for astigmatic axis location). The different performance in repeatability between keratometry and TMS-1 on highly astigmatic postoperative corneas, indicates that the two instruments should not be used interchangeably in these cases. Again, no previous studies have assessed vigorously intra- and inter-observer variability of videokeratography and keratometry on highly astigmatic human corneas. There are only the previously mentioned studies showing the decreased accuracy of videokeratography on test surfaces steeper or flatter than the normal corneas (*Hannush et al,* 1989; *Legeais et al,* 1993; *David & Dresner,* 1991) or on radially aspheric test surfaces (*Roberts,* 1994a) that could support the findings of the present study.

The present study has assessed the reproducibility of the TMS-1 and keratometry methods *in vivo.* The values obtained for the keratometer closely agree with the published literature. The performance of the videokeratography (TMS-1) was below the expectations arising from previous studies on test spherical surfaces, but this emphasises the difference between experiments on spheres and "the clinical situation". There are many possible explanations for the differences observed between the performance of the two instruments in this study. It should be also emphasised that the measurement disagreement could be even bigger if the recommended Zeiss index (1.332) was used for the keratometric calculations of power. We chose instead to use a uniform index (1.3375) to eliminate this source of bias.

TABLE 2.11 : Assumptions made by keratometer and CAVK [modified from *Corbett et al,* 1994b]

Assumptions	Kerat'y	CAVK
1) Corneal shape spherocylindrical	+	
2) Corneal surface locally spherical		+
3) Cornea of uniform refractive index	+	+
4) Neglects corneal thickness	+	+
5) Correct corneal position and orientation	+	+
6) Astigmatism effect neglected, so calculations can be made within a meridional plane		+
7) Centres of curvature for all reflected points are on the optical axis		+

Although keratometer and CAVK share some common assumptions [Table 2.11], they also differ in other respects. There are some sources of inaccuracy in CAVK that may arise from the instrument itself, or from the algorithms used. CAVK examines the air-tear film rather than the corneal surface itself (a limitation shared as well by keratometer). Irregularities of the tear film may cause incorrect measurements or missing data for computing, as it is the tear-film interface rather than the anterior corneal surface that is reconstructed. In this study it is highly unlikely that irregularities of the tear film are responsible for the differences between the two instruments in the normal corneas population, but it is possible that they have contributed to the variability of the results in the astigmatic post-PKP corneas group.

Accurate focusing is very important in obtaining reliable results with videokeratography. For the TMS-1, a 500 μm defocusing, has been calculated to produce an error up to 2.5 D for spheres of 60 D (*Mandell,* 1992). *Hannush et al.* (1989, 1990) believe that focusing techniques played significant role in the accuracy and precision differences among the instruments reported in their studies. In practice, it is true that due to the stromal scattering, blurring of the laser spots that the TMS-1 uses for focusing occurs, and this may complicate the accurate focusing. This phenomenon was observed throughout this study, but for the experienced observer it did not seem to represent a serious problem. However, as the focusing system of TMS-1 is relatively subjective, as it is dependent on the operator's judgement, it may well have contributed to the worse results seen with the novice observer. *Mandell* (1992) also found a considerable interobserver variation in the effort expended to achieve a perfect focus with the TMS. According to the same author, the EyeSys system has a less critical focusing problem due to the greater distance between instrument and target [Table 1.2]. However, *McCarey et al.* (1992) using the EyeSys system found that variations in focusing beyond 0.25 mm from the centre result in unreliable data, and results vary considerably on defocusing beyond the 1 mm. Furthermore, similar differences in results between keratometry and a device using autofocus feedback mechanism have been obtained (*Davis & Dresner,* 1991). On the other hand in the keratometer, incorrect focusing of the eyepieces of the instrument produces inaccuracies. This can produce an error in the radius reading as much as 0.4 mm (*Stone,* 1962). Additional inaccuracies of mechanical nature (backlash) can be caused by the possible amount of freedom of movement of the control knob before it operates the movable mechanism of the instrument (*Stone*, 1975). Although 'one position' keratometers in particular, tend to be quite incorrect for one of the two meridians because only one meridian can be at focus in toroidal corneas, the 10 SL/O Zeiss keratometer that was used in this study requires separate focusing for steep and flat meridians and therefore does not suffer from this disadvantage. The placement of the single cross centrally within the double cross as the instrument requires, is much less skill and experience related than the focusing of the TMS-1, although small inaccuracies can occur. Despite the fundamental limitations of the keratoscopic design, as errors can be introduced due to poor focus of different rings (*Ludlam et al,* 1966) if these are not on the same plane, TMS-1 manufactures claim that the patented cone [Figure 2.4] eliminates this problem. *Tsilimbaris et al.* (1991), using a system with a different keratoscope (EyeSys), suggested the observed differences in astigmatism were due to the problem in focusing of both principal meridians at the same time with the EyeSys in highly astigmatic corneas. *Legeais et al.* (1993) also suggested that the accuracy of the TMS could be improved by increasing the depth of field, and to achieve that a stronger illumination source with a higher sensitivity CCD camera could be used.

Correct alignment is also very important with videokeratography. In order for the CAVK to fulfil many of the assumptions made by the reconstructive algorithms, the cornea must be correctly positioned (*Wang et al,* 1991). Small errors in alignment can result in an irregular or asymmetric topographic reconstruction. In one commercially available instrument (EyeSys) poor fixation has been shown to produce a pattern of pseudokeratoconus; the increase in relative steepness was statistically significant at 5 degrees of deviation (*Hubbe & Foulks,* 1994). Therefore, errors in focusing and misalignment may have contributed to the novice observer variation compared to the experienced observer, as investigators not very familiar with the joystick alignment of the TMS-1 may be prone to slight decentrations and defocusing.

Potential inaccuracies in videokeratography can also arise from the algorithms used. There is no known mathematical formula which describes exactly the shape of the normal cornea; therefore the algorithm whatever it is, gives an approximation of the corneal shape. Current algorithms assume that the cornea is spherical, but algorithms that work well for spheres may not work for more complicated surfaces (*Maguire et al,* 1993). On the study with calibrated steel balls a clustering of deviation score values was noted on the positive side of zero for calibrated balls of 38 D, 43 D and 50 D. This suggests a systematic error in the interpretative computer algorithms (*Hannush et al,* 1989). A systematic error in algorithms could account for the observed bias on normal corneas between keratometry and TMS-1. Furthermore, although both instruments measure similar cord lengths, they may not measure exactly the same cord length. It seems actually that the keratometer requires the tangential image plane to be focused to achieve measurement (*Bennett & Rabbetts,* 1991), whereas it has been shown that CAVK does not accurately measure the instantaneous (tangential) radius of curvature of an ellipse (*Roberts,* 1994a). In the latter study, the maximum observer error with the EyeSys system was greater than 3 D at a radius of 4 mm for a surface with an apical radius of curvature of 7.5 mm and an eccentricity of 0.5. It was also concluded that the misalignment error is small compared to the inherent error due to a spherically-biased reconstruction algorithm. It is therefore possible that in the post-PKP corneas that exhibit high toricity, this is a major factor producing inaccuracies that may account for the differences seen between the two groups of patients. It seems likely that the more toric the surface the bigger is the error introduced. Finally the quality of the automatic digitisation in CAVK may play a role in the reproducibility of the instrument.

The measurement of the keratometer is also correct only when the surface measured is spherical or toroidal with the mires in the meridian planes of greatest or least curvature (*Clark,* 1973b). From Appendix III is seen that the central corneal curvature is measured between two points. An assumption is made that the surface between these two points is spherical. Depending on the shape factor deviation of the surface measured from that of a sphere, errors can be induced in the measurements. However, the clinical results of this study suggest that the introduced error in aspherical surfaces is smaller than in the TMS-1 and result in a better reproducibility with the keratometer.

This study was not designed to examine the relative contribution of all these possible factors to the observed findings. However, the possible explanations have been discussed.

2.6. Conclusions

There are a number of conclusions arising from this study which evaluated agreement and repeatability of methods commonly used to measure corneal contour in clinical settings.

In summary the following findings were documented :

1. There is a systematic bias of the TMS-1 towards the 10 SL/O Zeiss keratometer, in measuring steeper both principal meridians and higher amount of astigmatism in a constant basis, on normal corneas. However the two instruments demonstrated good agreement (clinically acceptable) in measuring the magnitude of astigmatism and the location of principal meridians on normal corneas.

2. In highly astigmatic post-PKP corneas, the systematic bias of the TMS-1 was more evident in measuring steep meridian power. Measuring disagreement between the two instruments was higher than in normal corneas for all the measured parameters, apart from meridian location agreement which was better.

3. Intra- and interobserver repeatability of the keratometer for normal corneas is excellent, at very acceptable clinical levels, and is not affected by observers'

experience. Compared to TMS-1, the keratometer showed superior repeatability on normal corneas. On the other hand TMS-1 repeatability is observer related. Better training improves the repeatability of measurement with this instrument. Intraobserver variation with the TMS-1 is also astigmatism related, and increases with increasing astigmatism.

4. On measuring highly astigmatic postkeratoplasty corneas, the keratometer becomes less repeatable than on normal corneas, but its repeatability remains at clinically acceptable levels for these irregular corneas. Compared to the TMS-1, the keratometer achieved superior reproducibility. The repeatability of the TMS-1 on post-PKP corneas was poor.

On the basis of the above findings it is finally concluded that the two instruments demonstrate clinically significant differences both on normal and astigmatic corneas, and therefore they should not be used interchangeably, especially when studying highly astigmatic corneas.

For the TMS-1, users of the same level of experience with the instrument should be employed in clinical or experimental studies.

CHAPTER 3

A PROPOSED CLASSIFICATION FOR TOPOGRAPHIC PATTERNS SEEN AFTER PENETRATING KERATOPLASTY

3.1. Introduction

Based on information obtained by keratometry, keratoscopy and photokeratoscopy, it is well documented that the shape of the anterior cornea is aspheric, radially asymmetric and that the position and size of the "central apical zone" is quite variable, as well as the rate of the peripheral flattening (*Knoll,* 1961; *Mandell & St Helen,* 1971; *Clark,* 1973a & 1974; *Kiely et al,* 1982).

The introduction of computer assisted photokeratoscopy (LSUCTS), provided theoretical advantages over the previously used methods for the assessment of the topography of normal corneas (*Dingeldein & Klyce,* 1989). In a later study conducted by *Bogan et al.* (1990), computer-assisted videokeratography (CMS, Computed Anatomy Inc, NY) was used for a qualitative classification of topography of normal corneas. This remains the most extensive study to-date of analysis of normal eyes topography with the assistance of CAVK. The authors evaluated the topography of 399 normal corneas and derived a qualitative classification system on the patterns seen with colour-coded topographic maps. All corneas were found to be steeper centrally and flatter peripherally. Five different patterns were recognised in colour-coded topographic maps. These were round in 22.6%, oval in 20.8%, symmetric bow tie in 17.5%, asymmetric bow tie in 32.1% and irregular in 7.1%. The authors suggested that the pattern types probably form a continuum. Recently, *Rabinowitz et al.* (1996) expanded this classification scheme to 10 subgroups to allow for a more detailed pattern analysis.

Bogan et al. (1991), extended their previous work by using computer assisted videokeratography (CMS) to classify the topography of post-radial keratotomy corneas based on the colour-coded maps and the cross section of the shape. One pattern not identified in normal eyes, polygonal, was noted in 59% of the corneas in their study, while in 70% the shape was oblate (flatter centrally than peripherally).

The previously reported classifications of normal and post-radial keratotomy corneas, are however inadequate for the great variability of topographic patterns with irregular astigmatism seen after penetrating keratoplasty.

To-date, to the best of my knowledge no classification scheme based on topographic patterns has been adopted for postkeratoplasty corneas. The great heterogeneity of the computer generated maps seen in corneas after PKP presents a challenge in classification.

3.2. Objectives of the present study

The study described in this chapter has the following objectives :

1) to classify qualitatively the patterns of corneal topography after penetrating keratoplasty.

2) to correlate topographic patterns with keratometric and refractive data and understand relationships if any, between different astigmatic topographic patterns and refractive errors.

3) to assess correlation of topographic patterns to specific preoperative diagnoses.

4) to monitor changes of topographic patterns over the postoperative period in a standardised manner.

The prevalence of topographic patterns in relation to different suturing techniques used in penetrating keratoplasty will be assessed in chapter 4, while the implication of the classification proposed here, in planning refractive surgery accordingly for high postkeratoplasty astigmatism, will also be evaluated later in chapter 5 (*vide infra*).

3.3. Materials and methods

3.3.1. *Selection of subjects*

Three hundred and sixty (360) corneal topographic pictures from 95 eyes (88 patients) who had undergone penetrating keratoplasty (PKP) were examined. Subjects included all those patients who were prospectively followed up in the third study (presented as chapter 4) of the present thesis. All patients were operated at Bristol Eye Hospital for a variety of indications (Table 4.3, chapter 4) and had received a donor button sutured with either of the two employed surgical techniques (a combination of 12 interrupted 10/0 Nylon and 12-bites continuous 11/0 Nylon suture, or a single continuous 24-bites 10/0 Nylon suture), as assigned by a random numbers table. At the time of examination, all cases were within twelve months from the date of PKP.

3.3.2. *Instrumentation*

The instruments used in this study were the TMS-1 (Computed Anatomy, New York, NY, software version 1.61) model of videokeratography, and the 10 SL/O model of keratometry (Carl Zeiss Ltd.). They have been described in detail in the materials and methods section of chapter 2 (2.3.1.2). Both devices had been calibrated before the beginning of the study and were periodically checked throughout the study, as described in chapter 2.3.3.

3.3.3. *Methods of examination*

All subjects underwent the following routine examinations : slit-lamp microscopy, manifest refraction, keratometry and videokeratography at every visit. Manifest refraction with the fogging technique and keratometry measurements were performed by a qualified optometrist; the videokeratographs were taken by either an ophthalmologist (CHK) or an optometrist trained in the use of videokeratography. The repeatability of these operators had been previously examined (chapter 2) and found to be very comparable. Slit-lamp microscopy of all patients was performed by the same ophthalmologist (CHK). All corneal topographic examinations, keratometry measurements and refraction were conducted in the same site, under standardised conditions of examination.

Applanation tonometry was not performed prior to keratometry or video-keratography. No artificial method for widening the palpebral aperture such as a lid speculum was used. No artificial tears were used to improve picture quality.

Three measurements from each cornea were obtained with both the keratometer and the TMS-1, on a manner described previously (chapter 2.3.3.). All three videokeratographs were processed. A gross assessment of repeatability was confirmed by comparing the "simk" readings of the three examinations. The best picture with the most information, least eyelid shadow to allow as many rings to be processed as possible, proper centration and absence of dry spots was selected. After processing, colour coded maps were obtained using the absolute scale.

Absolute & Normalised colour displays

On the *absolute scale* map, proposed by *Maguire et al.* (1987a) each colour represents always a specific dioptric power. This is according to the distribution of central corneal power among the normal population. The central corneal power has a Gausian distribution (*Corbett et al,* 1994a) with a mean of 43.50 D (range 39 D to 48 D), which is presented by light green/yellow colour in the TMS-1 instrument. The adjacent colours on the scale (orange and green) represent normal corneal powers. The colours at each extreme end of the scale (red and blue) are used for the extremes of corneal power seen in abnormal eyes. The range of curvatures on the absolute scale of TMS-1 is 9 to 100 D. The instrument uses 26 steps of colours; eleven 1.5 D steps are employed in the midrange (35.5 to 50.5 D), and 5 D steps are employed above (50.5 to 101.5 D) and below (9.0 to 35.5 D) the midrange.

CURVATURE	TMS-1 COLOURS
> 48 D (abnormally steep)	Red
47 D	Orange
44.5 D	Yellow
43 D (mean)	Light Green
40 D	Green
< 38 D (abnormally flat)	Blue

The fact that in absolute scale the same colours represent always the same dioptric power or curvature, allows comparison between different maps.
On the *normalised scale*, the intervals between colour steps are smaller than in the absolute scale. This provides more detailed information and higher resolution, but on the other hand can be misleading by overemphasising subtle changes in curvature. Furthermore it should not be used in comparative studies between pictures at different time or between different individuals, as the mean dioptric power whatever its value, is represented always with the same colour. An eleven equal steps spectrum of colours is then automatically adjusted by the instrument to fill the range of dioptric power at scales of a minimum 0.4 D for the TMS-1. The step size depends on the total range; if this is large, the steps will be large, and if the total range is small, the steps will be small. That also means that different values of dioptric powers between different pictures, are represented with the same colour.

3.3.4. *Selection of pictures for analysis*

All patients were seen at standardised postoperative intervals (3, 6, 9 and 12 months post-PKP) and for the purpose of the current study, the topographic maps taken at these time intervals were assessed. An equal number of topographic maps (four) for each eye were studied. In 8 of the 95 cases, less than four pictures were assessed, either because patients died during the follow up period, missed their appointment, or left the study for other reasons (rejection episode, graft failure). In these cases, data available up to the most recent follow up visit were evaluated.

3.3.5. *The proposed qualitative topography classification system*

Since there was no existing classification system for post-PKP corneas, a classification was derived by the author of this thesis after monitoring all post-PKP topographic maps during a two year period. Certain patterns of corneal topography were identifiable. The proposed classification was designed [Figure 3.1] with the aid of computer drawing software (Microsoft draw) and used throughout in the evaluation of the maps.

All 360 topographic maps were initially reviewed by the primary investigator (CHK) and classified according to the configuration of the colours obtained on the absolute scale. In a few instances, the normalised scale was used when classification of the map using the absolute scale was difficult. Although there was variability on the area of the cornea covered by the colour maps, they usually corresponded to the central and paracentral region of the cornea (the area occupied by the graft button itself). Whenever it was obvious that a certain area of the picture was attributed to the host cornea and not to the donor button itself (by superimposing the videokeratograph to the colour coded picture), this peripheral area was ignored.

Because of the qualitative nature of the system of classification, there was a risk of bias being introduced by the investigator. In order to reduce this bias, the following objective criteria were used for the categorisation and terminology of the classification.

A. The corneal shape : This refers to the contour of a cross-section of the cornea. In terms of corneal shape the examined corneas could be allocated to one of three categories : Prolate, oblate, or mixed.

1. ***Prolate*** : the cornea appears to have increased dioptric power (steeper) centrally than at the periphery [Figure 3.1]. This shape is also described as having a positive shape factor [appendix Ib].

2. ***Oblate*** : in this configuration the topographic pattern shows a cornea of decreased power (flatter) centrally than peripherally [Figure 3.1]. It is also described as a cornea with a negative shape factor [appendix Ib].

3. ***Mixed (prolate and oblate)*** : in this configuration features of both oblate and prolate shape are present at different corneal areas [Figure 3.1].

B. *The nature of astigmatism* : According to the characteristics of the astigmatism, this was classified as oval, regular (including oval) or irregular, symmetric or asymmetric.

1. ***Oval pattern*** : As defined by *Bogan et al.* (1990) in the classification of normal corneas, when the ratio of the shortest to the longest diameter at the colour zone chosen for pattern reading is less than 2/3, this configuration is called oval [Figure 3.1].

2. ***Regular astigmatism*** : This is the astigmatism found in toroidal corneas, where the two principal meridians of refraction are oriented at approximately right angles to each other. By definition oval astigmatism is a subclassification of the regular type of astigmatism. However, regular astigmatism is usually presented topographically by a bowtie pattern which can be symmetrical or asymmetrical [Figure 3.1]. The orientation of the bowtie indicates the axis of the plus cylinder. In our study regular astigmatism was defined as any astigmatism presenting with an angle α between the axis of the two halves of the bow-tie of less than 20^{o} [Figure 3.2].

2a. ***Regular symmetric bow-tie pattern*** : This type of regular astigmatism, in addition to the above mentioned criteria for regularity, shows also the following characteristics: *(a)* the ratio X_1/X_2 of the width of the two lobes of the bowtie [Figure 3.2] is 2/3 or more, and/or *(b)* the difference in power between the two limbs of the bow $|A-B|$ is 1 Dioptre or less, when measured with the TMS-1 cursor at a radius of 1.5 mm from centre .

2b. ***Regular asymmetric bow-tie pattern*** : A regular astigmatism was defined as asymmetric, when the following additional criteria were met : *(a)* X_1/X_2 ratio less than 2/3, and/or *(b)* $|A-B| > 1$ D [Figure 3.2]. Topographically this is presented as "ten-pin" shaped [Figure 3.1].

3. ***Irregular astigmatism*** : Some corneas show a much more complex geometry. If the axes showing the greatest difference in power were at an angle (α) to each

other greater than 20^o, this astigmatism was defined as irregular. This is represented topographically as a "bi-oblique" bowtie pattern [Figures 3.1 & 3.2].
A combination of the above criteria, resulted in the identification of five subclassifications of the regular astigmatism. These were : 1) (prolate) oval pattern [Figure 3.3B], 2) prolate symmetric bow-tie (PSBT) pattern [Figure 3.4A], 3) prolate asymmetric bow-tie (PABT) pattern [Figure 3.4B], 4) oblate symmetric bow-tie (OSBT) pattern [Figure 3.4C], and 5) oblate asymmetric bow-tie (OABT) pattern [Figure 3.4D]. Irregular astigmatism was subclassified accordingly into: 1) prolate irregular (PI) pattern [Figure 3.5A], 2) oblate irregular (OI) pattern [Figure 3.5C], and 3) mixed pattern [Figures 3.5B & 3.5D].

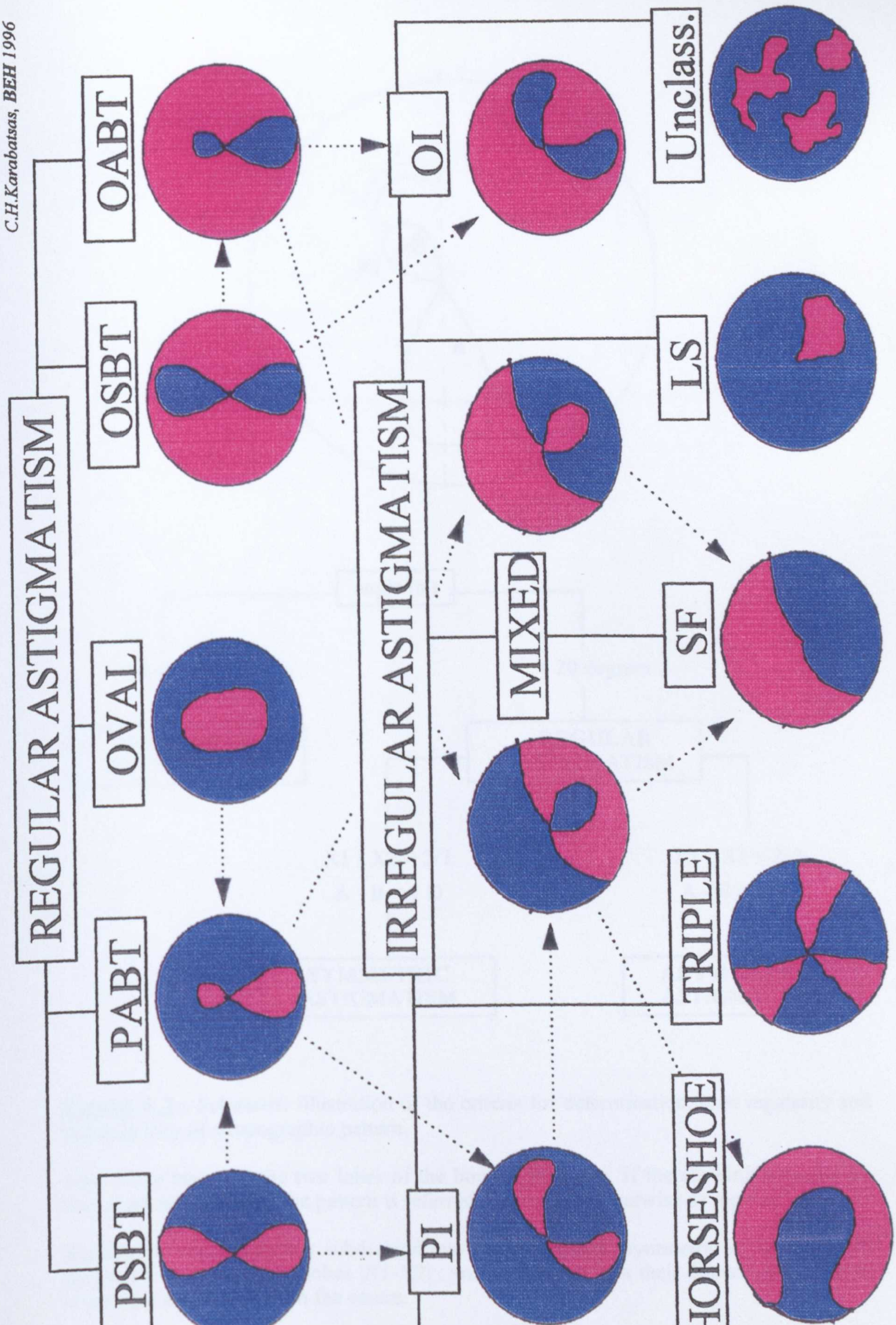
In addition to these, the following four characteristic patterns (subclassified under the irregular astigmatism) were identified, by objective criteria.
1. Steep/Flat (SF) pattern : In this group, the cornea was steeper on one side, becoming progressively flatter towards the other side [Figure 3.6A].
2. Localised steep (LS) pattern : In this pattern, an eccentric area of localised steepness, up to one quarter of corneal diameter size could be seen, surrounded by cornea of relatively lower power (flatter) [Figure 3.6B].
3. Triple pattern : Characteristically, three distinct areas of radial steepening were identifiable in a number of corneas [Figure 3.6C].
4. "Horseshoe" pattern : In this configuration, a petaloid area of increased corneal power could be identified at the graft-host interface [Figure 3.6D]. These corneas, by definition were of the oblate shape.
Finally, two more groups of maps were suggested by the classification; one including the "non-astigmatic" corneas [Figure 3.3A], and the "unclassified" group [Figure 3.6A & B]. Therefore, the final classification includes 14 patterns [Table 3.1, Figure 3.1].

A second ophthalmologist (SDC), after becoming familiar with the proposed classification, reviewed all topographic maps on the TMS-1 screen having next to the screen the drawing scheme [Figure 3.1] and printed examples

TABLE 3.1 : Patterns of the proposed classification for postkeratoplasty corneas

1. Non-astigmatic corneas
2. Regular astigmatism
   - (a) oval
   - (b) prolate symmetric bowtie (PSBT)
   - (c) prolate asymmetric bowtie (PABT)
   - (d) oblate symmetric bowtie (OSBT)
   - (e) oblate asymmetric bowtie (OABT)
3. Irregular astigmatism
   - (a) mixed
   - (b) prolate irregular (PI)
   - (c) oblate irregular (OI)
   - (d) "horseshoe" pattern
   - (e) "triple" pattern
   - (f) steep/flat (SF)
   - (g) localised steep (LS)
   - (h) unclassified

Figure 3.1 : The proposed videokeratography pattern classification scheme. PSBT : Prolate Symmetric Bow-tie, PABT : Prolate Asymmetric Bow-tie, OSBT : Oblate Symmetric Bow-tie, OABT : Oblate Asymmetric Bow-tie, PI: Prolate Irregular, OI : Oblate Irregular, SF : Steep / Flat, LS : Localised steep.
Most of the patterns can be seen as a continuum, with some of them changing into different patterns (arrows) after manipulation of post-PKP astigmatism, by removal or adjustment of sutures.


C.H.Karabatsas, BEH 1996
REGULAR ASTIGMATISM
PSBT
PABT
OVAL
OSBT
OABT
IRREGULAR ASTIGMATISM
PI
MIXED
OI
HORSESHOE
TRIPLE
SF
LS
Unclass.

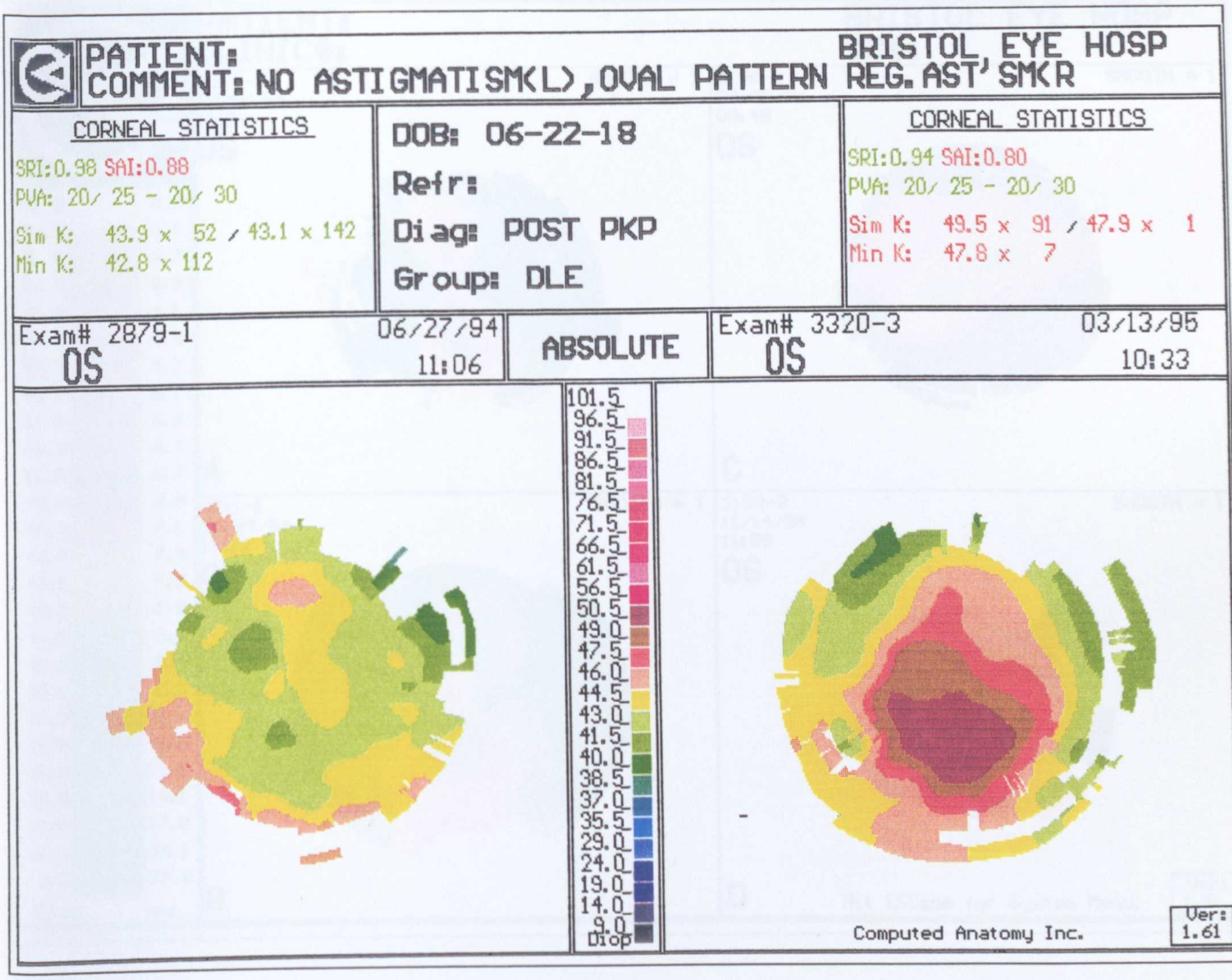
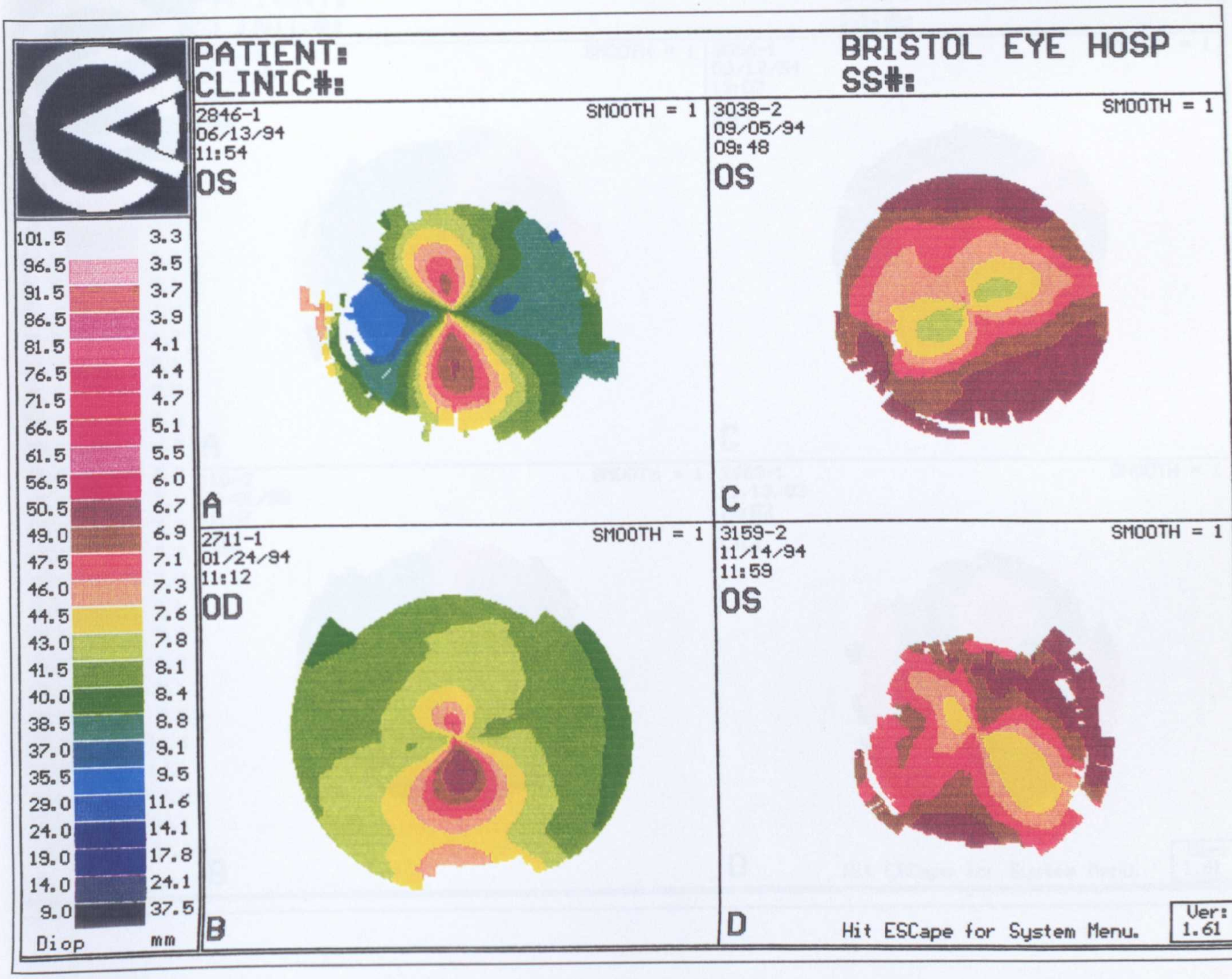


Figure 3.3 : Examples of videokeratographic patterns

A (left) : Non astigmatic cornea

B (right) : Oval (prolate) astigmatic pattern with central area of steepening.



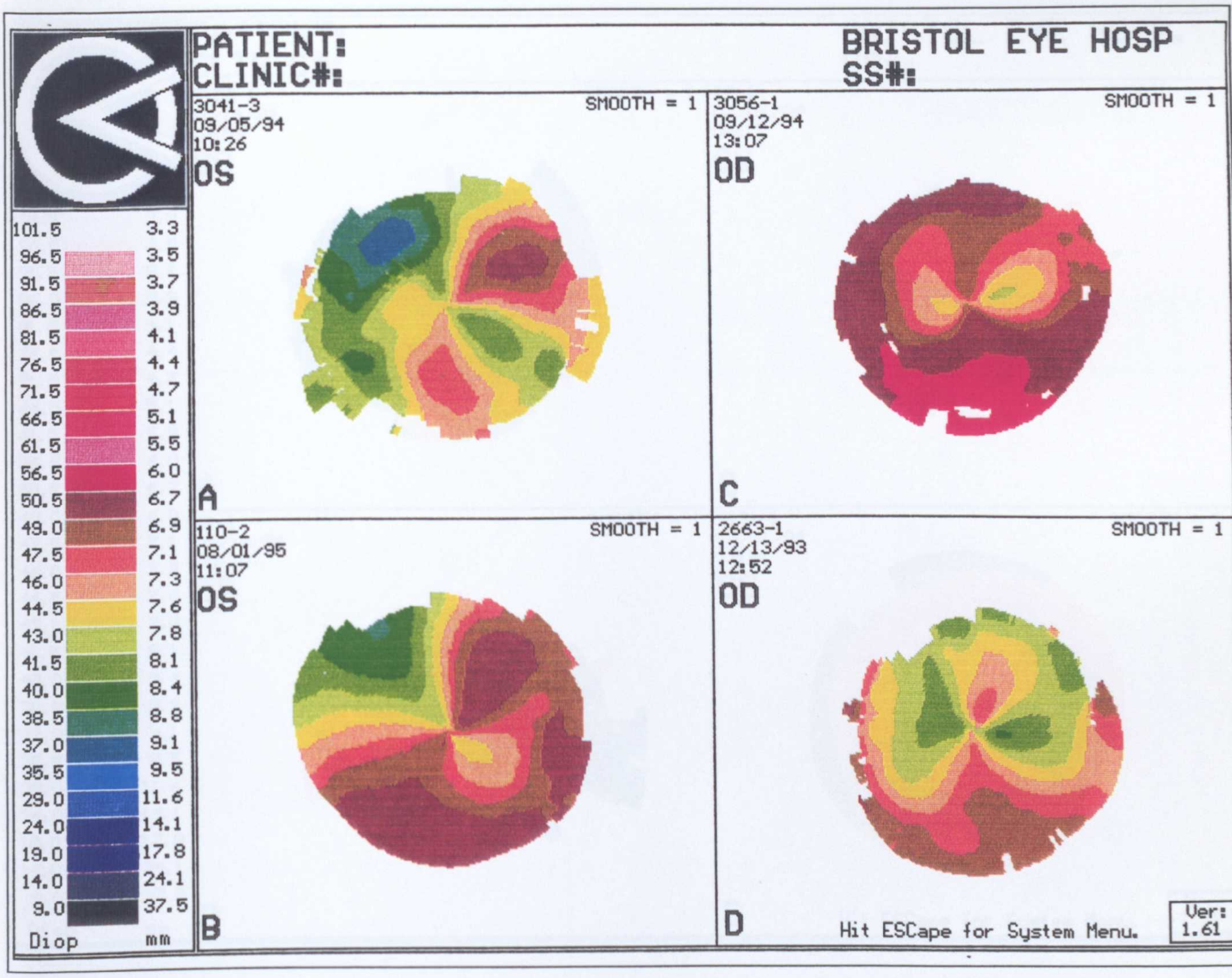
<u>Figure 3.4</u> : Examples of different topographic patterns of regular astigmatism

<u>A</u> (top left) : Prolate symmetric bowtie (PSBT) pattern

<u>B</u> (bottom left) : Prolate asymmetric bowtie (PABT) pattern

<u>C</u> (top right) : Oblate symmetric bowtie (OSBT) pattern

<u>D</u> (bottom right) : Oblate asymmetric bowtie (OABT) pattern

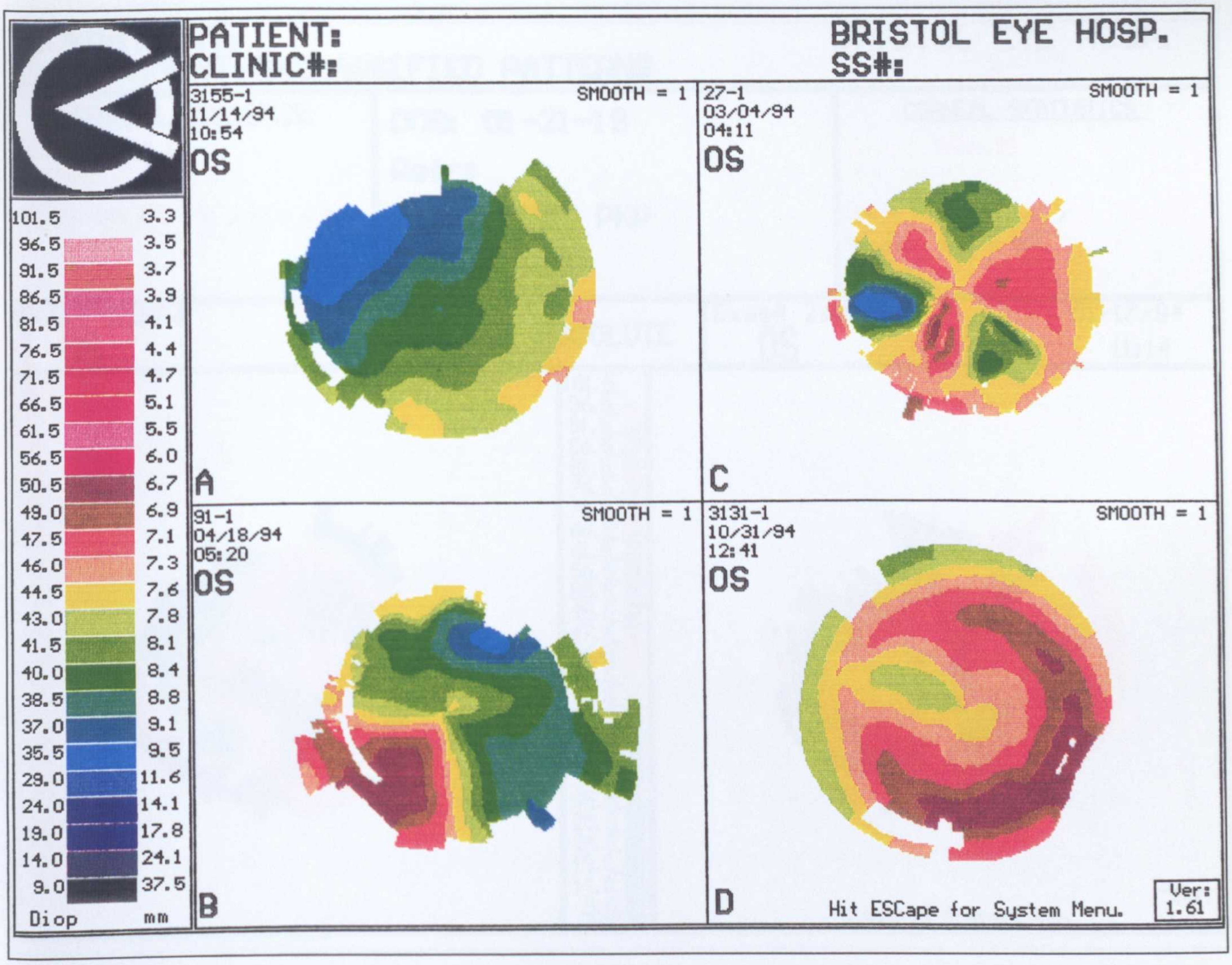


<u>**Figure 3.5**</u> : Examples of different topographic patterns of irregular astigmatism

<u>A</u> (top left) : Prolate irregular (PI) pattern

<u>C</u> (top right) : Oblate irregular (OI) pattern

<u>B & D</u> (bottom left & right) : mixed irregular patterns



<u>Figure 3.6</u> : Examples of different topographic patterns of irregular astigmatism

<u>A</u> (top left) : Steep/flat (SF) pattern

<u>B</u> (bottom left) : Localised steep (LS) patterns

<u>C</u> (top right) : Triple pattern

<u>D</u> (bottom right) : "horseshoe" pattern

3.3.6 . *Quantitative indices*

On all videokeratographs, the following quantitative indices were recorded : *(a)* simulated keratometry readings (simk), *(b)* surface regularity index (SRI), and *(c)* surface asymmetry index (SAI). These indices have been described in detail previously (chapter 2).

3.3.7 . *Data collection and statistical analysis*

All data (quantitative indices and qualitative classification after picture review) were entered into an Excel spreadsheet (Microsoft, Seattle, WA). Files were then statistically analysed with the Minitab statistics package, version 10.X (Minitab Inc, Reading, MA) on an IBM compatible computer.

For the different pattern subgroups (categorical data) separate analysis was performed for each time point (3, 6, 9 and 12 months post-PKP) to assess the impact of time post-surgery on corneal topography. Fisher's exact test was used to compare between keratoconic and non-keratoconic groups.

For measurements of astigmatism (keratometric, refractive, topographic astigmatism, as well as SAI and SRI measurements) among topographic groups, only the 12 months data [Table 3.8] were analysed. Small numbers (<5) in some of the non-astigmatic stratified groups did not permit meaningful statistical analysis for these groups alone. Therefore, differences in means were compared with distribution free statistical techniques (Kruskal-Wallis test) for the rest of the subgroup comparisons. Differences between the pooled regular and irregular groups for which suitable sample sizes are available, were tested with the one - way ANOVA test. Statistical significance for all tests was at the 0.05 level.

3.4. Results

Demographic data for the 95 post-PKP eyes (88 patients) that were evaluated are found in the results section of chapter 4. The total number of topographic maps that were analysed and classified in this series was 360. Of these, 7 maps were considered by both examiners as pictures of very poor quality, where no reliable data could be obtained. Therefore the final number of topographic maps left for classification was three hundred and fifty-three (353).

3.4.1. Agreement between examiners

All the topographic images were independently classified by the two observers. Exact agreement was achieved in 309/353 cases (87.5%). Disagreements were then reviewed by both observers together, and a consensus grade was agreed for a further 13 images following discussion. The total number of agreed grades was thus 322/353 or 91.2%.

3.4.2. Distribution of topographic patterns

The percentage of the total sample group of 353 maps, comprising each pattern is shown in Table 3.2. There were 10 topographic maps showing no astigmatism (2.8%), while 106 videokeratographs (30%) showed characteristics of regular astigmatism. The regular astigmatic patterns were subclassified as : topographic maps with an oval pattern in 14 cases (4%), prolate symmetric bow-tie (PSBT) in 12 cases (3.4%), prolate asymmetric bow-tie (PABT) in 39 cases (11%), oblate symmetric bow-tie (OSBT) in 13 cases (3.7%) and oblate asymmetric bow-tie (OABT) in 28 cases (7.9%). Irregular astigmatic patterns were seen in 206 cases (58.4%), subclassified as : Prolate irregular (PI) pattern in 38 videokeratographs (10.8%), oblate irregular (OI) in 8 cases (2.3%), mixed pattern in 22 cases (6.3%), steep/flat (SF) pattern in 38 maps (10.8%), localised steepness (LS) in 44 cases (12.5%), triple pattern was recognised in 15 topographic maps (4.2%), "horseshoe" pattern in 9 cases (2.6%), whereas 32 topographic maps (9%) could not be classified in any of the above groups. Of the topographic maps, 113 (32%) had a prolate configuration (non astigmatic, oval, PSBT, PABT, PI); 58 (16.5%) showed an oblate configuration (OSBT, OABT, OI, horseshoe pattern); and 151 videokeratographs (42.8%) showed a mixed prolate/oblate configuration (unclassified, mixed, SF, LS, triple).

3.4.3. Change in topographic patterns over time

Distributions of the various patterns at the 3, 6, 9 and 12 months post-PKP intervals are shown on Table 3.3. Depending on the time interval when topography is examined, regular astigmatism was present in a percentage between 23.5% (at 12 months post-PKP) and 39.1% (at 3 months post-PKP). The percentage of irregular astigmatism was between 60.7% (at 9 months) and 71.8% (at 12 months post-PKP). Although the percentages of regular and irregular astigmatism remain quite stable over the first 9 months post-PKP, at the 12-month follow up visit an increase of the irregular astigmatism percentage is noted (from 60.7% at 9-months, to 71.8% at 12-months), together with an associated decrease of the combined regular patterns (from 34.5% at 9-months to 23.5% at 12-months). This is illustrated in figure 3.8. At the 12-months follow up visit (n=85), 4.7% of the corneas showed no astigmatism, 3.5% showed oval pattern, 7% showed PABT and OSBT patterns, but no map was identified with PSBT pattern. Of the irregular astigmatic patterns, the most common was the LS (18.8%), followed by the SF pattern (12.9%); 5.9% of the corneas had PI pattern, 4.7% had OI pattern, 8.2% mixed, 3.5% showed triple and horseshoe pattern, and 14.1% were unclassified [Table 3.3].

3.4.4. Correlation of topographic patterns to preoperative diagnosis

Distribution of the topographic patterns was also examined according to preoperative diagnosis (with patients divided into keratoconic and non-keratoconic), and time interval following PKP [Tables 3.2, and 3.4 to 3.7]. At 3 months post-PKP the only statistically significant difference in topographic patterns distribution between the two groups was for the SF pattern [Table 3.4], which was more often seen in non-keratoconic patients ($p<0.01$, Fisher's exact test). At 6 months post-PKP, LS was significantly more common between non-keratoconic patients than in patients with keratoconus; irregular astigmatic patterns were also more commonly seen ($p<0.01$) in non-keratoconic corneas, whereas OABT was the pattern seen significantly more often in keratoconic than non-keratoconic corneas [Table 3.5]. The same difference in distribution continued at the 9 months interval, where also the regular astigmatism reaches significance between the two groups (regular astigmatism seen more commonly in keratoconic than non-keratoconic patients, Table 3.6). An additional finding at 12 months [Table 3.7] is the presence of significantly more mixed and non-astigmatic patterns among keratoconic patients, whereas the difference in regular astigmatic patterns is not significant any more between the two groups of patients.

3.4.5. Correlation of topographic patterns to suturing techniques

This correlation is assessed in the next chapter 4.

3.4.6. Relationship between topographic patterns and astigmatism

To test for correlation between topographic patterns and astigmatism, the 12 months topographic patterns were considered [Table 3.8]. Small numbers ($n<5$) for some stratified topographic patterns (non-astigmatic, oval, OI, triple and horseshoe), did not permit meaningful statistical analysis for these groups alone.

Refractive astigmatism (cyl D) : Distribution free statistical techniques (Kruskal-Wallis test) demonstrated that for refractive astigmatism there was no statistically significant difference ($p=0.244$) among subgroups of topographic patterns. The least refractive astigmatism was in the triple pattern (mean ± SD, 1.25 ± 0.66) and in the non-astigmatic pattern (1.62 ± 0.85). The most refractive astigmatism was recorded in the OABT pattern (5.35 ± 4.47). The pooled regular astigmatism group was also not found to be different from the pooled irregular astigmatism group in terms of refractive astigmatism ($p=0.175$, ANOVA).

Keratometric astigmatism : There were no statistically significant differences among topographic patterns when tested separately ($p=0.476$, Kruskal-Wallis test), or as pooled broader categories ($p=0.185$, ANOVA for combined regular vs. irregular astigmatism). Apart from the non-astigmatic group, the horseshoe pattern was the one that showed the least keratometric astigmatism (2.0 ± 0.69 D). The most keratometric astigmatism was recorded in the OI pattern (7.2 ± 2.23 D) and the OABT pattern (6.93 ± 5.90 D).

Topographic astigmatism (simk) : No differences in mean topographic astigmatism among the subgroups with adequate sample size were found (p=0.368, Kruskal-Wallis test). Among subgroups, OABT pattern showed the most topographic astigmatism (6.84 ± 4.83 D), whereas horseshoe (1.63 ± 0.30 D) and non-astigmatic patterns (1.9 ± 1.15 D) the least.

However, when tested as pooled groups, the regular and irregular astigmatic groups were different (p=0.05, ANOVA), with the regular astigmatism exhibiting greater values (5.09 ± 4.12 vs. 3.70 ± 2.15, Table 3.8).

3.4.7. Relationship between topographic patterns and quantitative indices

SRI : Kruskal-Wallis test analysis indicated that there were differences among some of the topographic groups for SRI (p=0.04)[1]. Moreover, although SRI was lower in the pooled regular astigmatic group (1.24 ± 0.83) than in the pooled irregular astigmatic group (1.70 ± 1.37), the difference between the two groups was not significant (p=0.15, ANOVA).

SAI : For SAI measurements, there were statistically significant differences among stratified topographic groups when tested separately (p=0.007, Kruskal-Wallis test) or as pooled broader categories (regular vs. irregular patterns, F=3.69, p=0.05, ANOVA). SAI was less for the regular astigmatic patterns than for the irregular ones (0.91 ± 0.59 vs. 1.23 ± 0.65, Table 3.8). Furthermore, when comparing the combined 'symmetric astigmatic group' (PSBT and OABT) against the 'asymmetric astigmatic group' (PABT and OABT), the difference was approaching statistical significance (p=0.06 with -0.09, 0.84 96.1% C.I. for the difference, Mann-Whitney test).

[1] small numbers however on each individual subgroup (n<10) do not permit a follow up analysis with the Wilcoxon signed rank method (*Brown & Swanson Beck*, 1994).

TABLE 3.2 : Distribution of the topographic patterns in 353 post-PKP video-keratographs, according to preoperative diagnosis

Topographic pattern	Keratoconus	Non keratoconic	Total
I. NON ASTIGMATIC	8 (5.5%)	2 (1%)	10 (2.8%)
II. REGULAR ASTIGMATISM	57 (39.3%)	49 (23.6%)	106 (30%)
Oval	3 (2%)	11 (5.3%)	14 (4%)
PSBT	5 (3.4%)	7 (3.4%)	12 (3.4%)
PABT	18 (12.4%)	21 (10%)	39 (11%)
OSBT	8 (5.5%)	5 (2.4%)	13 (3.7%)
OABT	23 (16%)	5 (2.4%)	28 (7.9%)
III. IRREGULAR ASTIGMATISM	73 (50.3%)	133 (64%)	206 (58.4%)
PI	15 (10.3%)	23 (11%)	38 (10.8%)
OI	4 (2.8%)	4 (1.9%)	8 (2.3%)
Mixed	10 (6.9%)	12 (5.8%)	22 (6.3%)
SF	11 (7.6%)	27 (13%)	38 (10.8%)
LS	9 (6.2%)	35 (16.8%)	44 (12.5%)
Triple	8 (5.5%)	7 (3.4%)	15 (4.2%)
Horseshoe pattern	4 (2.8%)	5 (2.4%)	9 (2.6%)
Unclassified	12 (8.3%)	20 (9.6%)	32 (9%)
Non agreement	7 (4.8%)	24 (11.5%)	31 (8.8%)
Total	145	208	353

TABLE 3.3 : Distribution of topographic patterns seen at different time intervals post-PKP*

Topographic patterns	3 m'ths No.(%)	6 m'ths No.(%)	9 m'ths No.(%)	12 m'ths No.(%)
I. NON ASTIGMATIC	-	2 (2.2)	4 (4.8)	4 (4.7)
II. REGULAR ASTIGMATISM	36(39.1)	32(34.8)	29(34.5)	20(23.5)
Oval	4 (4.3)	3 (3.3)	6 (7.1)	3 (3.5)
PSBT	5 (5.4)	7 (7.6)	2 (2.4)	-
PABT	16(17.4)	11 (12)	8 (9.5)	6 (7)
OSBT	2 (2.2)	-	5 (5.9)	6 (7)
OABT	9 (9.8)	11 (12)	8 (9.5)	5 (5.9)
III. IRREGULAR ASTIGMATISM	56(60.9)	58 (63)	51(60.7)	61(71.8)
PI	16(17.4)	9 (9.8)	10(11.9)	5 (5.9)
OI	-	2 (2.2)	2 (2.4)	4 (4.7)
Mixed	6 (6.5)	3 (3.3)	7 (8.3)	7 (8.2)
SF	8 (8.7)	12 (13)	9(10.7)	11(12.9)
LS	11(11.9)	15(16.3)	8 (9.5)	16(18.8)
Triple	7 (7.6)	6 (6.5)	3 (3.6)	3 (3.5)
Horseshoe pattern	1 (1)	2 (2.2)	3 (3.6)	3 (3.5)
Unclassified	7 (7.6)	9 (9.8)	9(10.7)	12(14.1)
Total number	92	92	84	85

* For maps where no agreement was obtained, the classification of investigator 1 was considered

TABLE 3.2 : Distribution of the topographic patterns in 353 post-PKP video-keratographs, according to preoperative diagnosis

Topographic pattern	Keratoconus	Non keratoconic	Total
I. NON ASTIGMATIC	8 (5.5%)	2 (1%)	10 (2.8%)
II. REGULAR ASTIGMATISM	57 (39.3%)	49 (23.6%)	106 (30%)
Oval	3 (2%)	11 (5.3%)	14 (4%)
PSBT	5 (3.4%)	7 (3.4%)	12 (3.4%)
PABT	18 (12.4%)	21 (10%)	39 (11%)
OSBT	8 (5.5%)	5 (2.4%)	13 (3.7%)
OABT	23 (16%)	5 (2.4%)	28 (7.9%)
III. IRREGULAR ASTIGMATISM	73 (50.3%)	133 (64%)	206 (58.4%)
PI	15 (10.3%)	23 (11%)	38 (10.8%)
OI	4 (2.8%)	4 (1.9%)	8 (2.3%)
Mixed	10 (6.9%)	12 (5.8%)	22 (6.3%)
SF	11 (7.6%)	27 (13%)	38 (10.8%)
LS	9 (6.2%)	35 (16.8%)	44 (12.5%)
Triple	8 (5.5%)	7 (3.4%)	15 (4.2%)
Horseshoe pattern	4 (2.8%)	5 (2.4%)	9 (2.6%)
Unclassified	12 (8.3%)	20 (9.6%)	32 (9%)
Non agreement	7 (4.8%)	24 (11.5%)	31 (8.8%)
Total	145	208	353

TABLE 3.3 : Distribution of topographic patterns seen at different time intervals post-PKP*

Topographic patterns	3 m'ths No.(%)	6 m'ths No.(%)	9 m'ths No.(%)	12 m'ths No.(%)
I. NON ASTIGMATIC	-	2 (2.2)	4 (4.8)	4 (4.7)
II. REGULAR ASTIGMATISM	36(39.1)	32(34.8)	29(34.5)	20(23.5)
Oval	4 (4.3)	3 (3.3)	6 (7.1)	3 (3.5)
PSBT	5 (5.4)	7 (7.6)	2 (2.4)	-
PABT	16(17.4)	11 (12)	8 (9.5)	6 (7)
OSBT	2 (2.2)	-	5 (5.9)	6 (7)
OABT	9 (9.8)	11 (12)	8 (9.5)	5 (5.9)
III. IRREGULAR ASTIGMATISM	56(60.9)	58 (63)	51(60.7)	61(71.8)
PI	16(17.4)	9 (9.8)	10(11.9)	5 (5.9)
OI	-	2 (2.2)	2 (2.4)	4 (4.7)
Mixed	6 (6.5)	3 (3.3)	7 (8.3)	7 (8.2)
SF	8 (8.7)	12 (13)	9(10.7)	11(12.9)
LS	11(11.9)	15(16.3)	8 (9.5)	16(18.8)
Triple	7 (7.6)	6 (6.5)	3 (3.6)	3 (3.5)
Horseshoe pattern	1 (1)	2 (2.2)	3 (3.6)	3 (3.5)
Unclassified	7 (7.6)	9 (9.8)	9(10.7)	12(14.1)
Total number	92	92	84	85

* For maps where no agreement was obtained, the classification of investigator 1 was considered

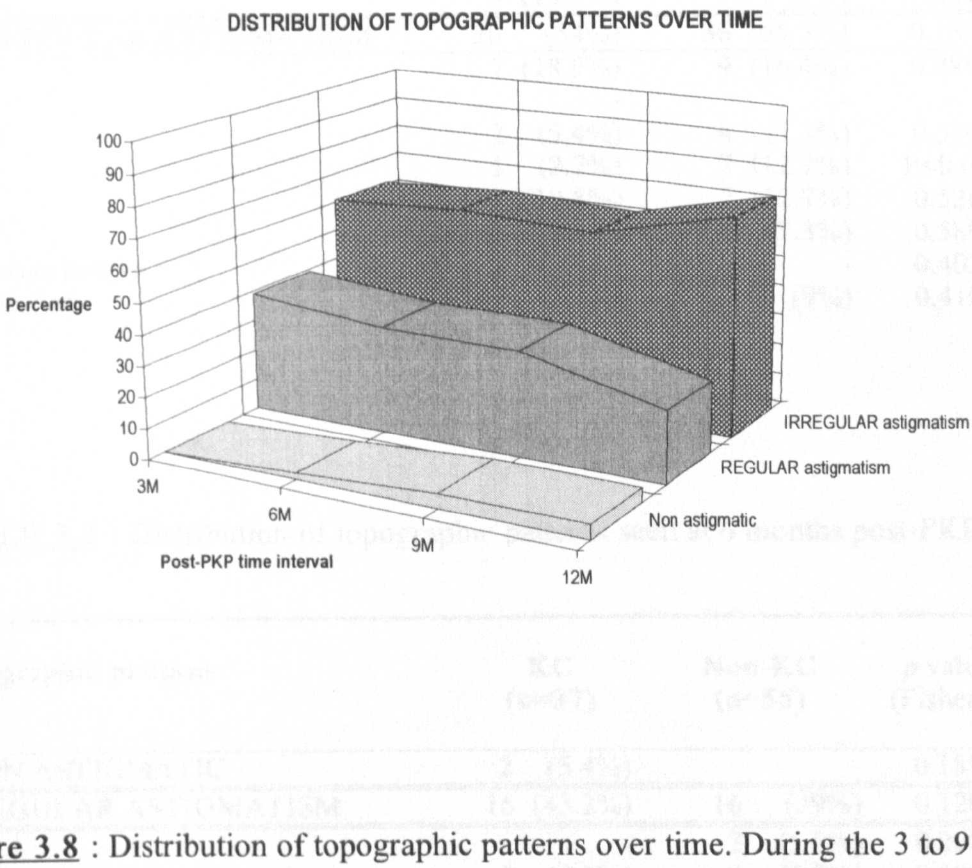


Figure 3.8 : Distribution of topographic patterns over time. During the 3 to 9 months post-PKP time interval, regular to irregular astigmatic patterns ratio is 1:1.5 at 3 months post-PKP, 1:1.8 at 6 months and 1:1.7 at 9 months post-PKP. At 12 months post-PKP however, the ratio of regular to irregular patterns is 1:3.

TABLE 3.4 : Distribution of topographic patterns seen at 3 months post-PKP

Topographic patterns	KC (n=37)	Non-KC (n=55)	*p* value (Fisher's)
I. NON ASTIGMATIC	-	-	-
II. REGULAR ASTIGMATISM	17 (46%)	19 (34.5%)	0.189
Oval	2 (5.4%)	2 (3.6%)	0.530
PSBT	1 (2.7%)	4 (7.3%)	0.327
PABT	8 (21.6%)	8 (14.5%)	0.272
OSBT	1 (2.7%)	1 (1.8%)	0.645
OABT	5 (13.5%)	4 (7.3%)	0.261
III. IRREGULAR ASTIGMATISM	20 (54%)	36 (65.5%)	0.189
PI	7 (18.9%)	9 (16.4%)	0.480
OI	-	-	-
Mixed	2 (5.4%)	4 (7.3%)	0.539
SF	1 (2.7%)	7 (12.7%)	P<0.01
LS	4 (10.8%)	7 (12.7%)	0.526
Triple	3 (8.1%)	4 (7.3%)	0.589
Horseshoe pattern	1 (2.1%)	-	0.402
Unclassified	2 (5.4%)	5 (9%)	0.410

TABLE 3.5 : Distribution of topographic patterns seen at 6 months post-PKP

Topographic patterns	KC (n=37)	Non-KC (n=55)	*p* value (Fisher's)
I. NON ASTIGMATIC	2 (5.4%)	-	0.159
II. REGULAR ASTIGMATISM	16 (43.2%)	16 (29%)	0.120
Oval	-	3 (5.5%)	0.208
PSBT	3 (8.1%)	4 (7.3%)	0.589
PABT	5 (13.5%)	6 (10.9%)	0.473
OSBT	-	-	-
OABT	8 (21.6%)	3 (5.5%)	P<0.01
III. IRREGULAR ASTIGMATISM	19 (51.4%)	39 (71%)	P<0.01
PI	3 (8.1%)	6 (10.9%)	0.474
OI	1 (2.7%)	1 (1.8%)	0.645
Mixed	-	3 (5.5%)	0.208
SF	4 (10.8%)	8 (14.5%)	0.424
LS	2 (5.4%)	13 (23.6%)	P<0.01
Triple	4 (10.8%)	2 (3.6%)	0.174
Horseshoe pattern	1 (2.7%)	1 (1.8%)	0.645
Unclassified	4 (10.8%)	5 (9%)	0.525

KC = Keratoconic patients; Non-KC = Non-keratoconic patients

TABLE 3.6 : Distribution of topographic patterns seen at 9 months post-PKP

Topographic patterns	KC (n=35)	Non-KC (n=49)	*p* value (Fisher's)
I. NON ASTIGMATIC	2 (5.7%)	2 (4%)	NS
II. REGULAR ASTIGMATISM	16 (45.7%)	13 (26.6%)	P<0.01
Oval	1 (2.9%)	5 (10.2%)	NS
PSBT	1 (2.9%)	1 (2%)	NS
PABT	3 (8.6%)	5 (10.2%)	NS
OSBT	3 (8.6%)	2 (4%)	NS
OABT	8 (22.8%)	-	P<0.01
III. IRREGULAR ASTIGMATISM	17 (48.6%)	34 (69.4%)	P<0.01
PI	4 (11.4%)	6 (12.2%)	NS
OI	1 (2.9%)	1 (2%)	NS
Mixed	2 (5.7%)	5 (10.2%)	NS
SF	3 (8.6%)	6 (12.2%)	NS
LS	1 (2.9%)	7 (14.3%)	P<0.01
Triple	2 (5.7%)	1 (2%)	NS
Horseshoe pattern	1 (2.9%)	2 (4%)	NS
Unclassified	3 (8.6%)	6 (12.2%)	NS

TABLE 3.7: Distribution of topographic patterns seen at 12 months post-PKP

Topographic patterns	KC (n=36)	Non-KC (n=49)	*p* value (Fisher's)
I. NON ASTIGMATIC	4 (11.1%)	-	P<0.01
II. REGULAR ASTIGMATISM	10 (27.8%)	10 (20.4%)	NS
Oval	-	3 (6.1%)	NS
PSBT	-	-	NS
PABT	2 (5.5%)	4 (8.2%)	NS
OSBT	4 (11.1%)	2 (4%)	NS
OABT	4 (11.1%)	1 (2%)	P<0.01
III. IRREGULAR ASTIGMATISM	22 (61.1%)	39 (79.5%)	P<0.01
PI	1 (2.8%)	4 (8.2%)	NS
OI	2 (5.5%)	2 (4%)	NS
Mixed	6 (16.7%)	1 (2%)	P<0.01
SF	3 (8.4%)	8 (16.3%)	NS
LS	3 (8.4%)	13 (26.5%)	P<0.01
Triple	2 (5.5%)	1 (2%)	NS
Horseshoe pattern	1 (2.8%)	2 (4%)	NS
Unclassified	4 (11.1%)	8 (16.3%)	NS

KC = Keratoconic patients; Non-KC = Non-keratoconic patients

TABLE 3.8 : Comparison of topographic patterns, in relation to astigmatism and quantitative indices.

Topographic pattern	Mean refractive astigmatism (D)	Mean keratometric astigmatism (D)	Mean topographic astigmatism (simk)	Mean SRI	Mean SAI
I. NON ASTIGMATIC	1.67 (SD:0.76)	1.17 (SD:0.99)	1.61 (SD:0.85)	0.82 (SD:0.39)	0.60 (SD:0.27)
II. REGULAR ASTIGMATISM	4.20 (SD:2.98)	5.08 (SD:3.21)	5.93 (SD:3.92)	1.63 (SD:1.26)	0.97 (SD:0.61)
Oval	2.17 (SD:1.22)	2.96 (SD:3)	2.70 (SD:1.97)	1.61 (SD:1.32)	1.06 (SD:0.49)
PSBT	4.09 (SD:1.81)	7 (SD:2.57)	8.18 (SD:4.63)	1.82 (SD:1.04)	1.01 (SD:0.54)
PABT	4.41 (SD:3.50)	5.45 (SD:2.76)	6.22 (SD:3.28)	2.07 (SD:1.48)	1.20 (SD:0.76)
OSBT	4.81 (SD:2.99)	4.63 (SD:3.70)	6.82 (SD:5.79)	1.08 (SD:0.59)	0.73 (SD:0.59)
OABT	4.62 (SD:2.79)	5.65 (SD:3.17)	5.72 (SD:2.88)	1.49 (SD:1.24)	0.90 (SD:0.38)
III. IRREGULAR ASTIGMATISM	3.37 (SD:2.38)	4.03 (SD:2.87)	3.98 (SD:2.47)	2.06 (SD:1.67)	1.44 (SD:0.88)
Prolate Irregular (PI)	4.61 (SD:2.49)	5.37 (SD:3.14)	5.20 (SD:2.49)	1.78 (SD:1.25)	1.09 (SD:0.57)
Oblate Irregular (OI)	5.46 (SD:1.51)	6.47 (SD:2.07)	5.70 (SD:2.64)	2.50 (SD:2.21)	1.22 (SD:0.98)
Mixed	4.22 (SD:2.92)	5.56 (SD:3.66)	4.83 (SD:2.73)	1.96 (SD:1.82)	1.19 (SD:0.77)
Steep/Flat (SF)	2.39 (SD:1.62)	2.87 (SD:1.39)	3.43 (SD:1.87)	1.96 (SD:1.79)	1.70 (SD:0.99)
Localised Steep (LS)	2.50 (SD:1.77)	3.02 (SD:2.14)	3.34 (SD:2.57)	2.10 (SD:1.57)	1.68 (SD:0.82)
Triple	3.78 (SD:2.95)	2.91 (SD:0.61)	2.70 (SD:1.54)	1.11 (SD:0.38)	0.94 (SD:0.47)
Horseshoe	2.08 (SD:1.61)	2.20 (SD:0.82)	2.26 (SD:1.25)	0.97 (SD:0.54)	0.97 (SD:0.42)
Unclassified	3.37 (SD:2.35)	4.58 (SD:3.91)	4.23 (SD:2.43)	3.19 (SD:1.92)	1.78 (SD:1.12)

3.5. Discussion

This study provides a new classification for the spectrum of topographic patterns seen in postkeratoplasty corneas. An acceptable observer agreement level of 87.5% was shown with the first review of the topographic images. The database of the corneas examined in this series is representative of the PKP population, as it includes individuals with a variety of preoperative diagnoses, different ages and sex, a variety of astigmatism amplitude, while donor buttons had been sutured during surgery with a variety of techniques.

Three previous studies have described the variations in videokeratographic patterns existing in normal corneas. *Dingeldein & Klyce* (1989) were first to report the variations of shape found in 44 normal corneas of 22 individuals, as revealed in maps generated by photokeratoscopy. Their study confirmed that all the examined corneas were steeper centrally and flattened progressively towards the periphery. The study revealed also variations in topographic patterns and central power among normal subjects, but failed to demonstrate the existence of an anatomical "apical corneal cap" as had been proposed earlier by *Aubert* (1885). Another finding was the high degree of mirror image symmetry often seen between the right and left eyes of the same individual. A good correlation (r=0.96) between photokeratoscopy and keratometry in measuring central corneal power, was also found. Soon afterwards *Bogan et al.* (1990) presented their classification of the topography of normal corneas based on a study of 399 eyes of 212 subjects. Using the normalised scale, they described five different patterns of colour-coded topographic maps : round in 22.6%, oval in 20.8%, symmetrical bow tie in 17.5%, asymmetric bow tie in 32.1% and irregular in 7.1%. *Rabinowitz et al.* (1996) expanded this scheme to 10 subgroups, in addition to using the absolute scale for their classification. The authors introduced additional quantitative indices (central K, I-S value, R versus L index, CA point, C-P index, AD), both for classification purposes and to facilitate detection of early keratoconus. However, the versatility of these indices in everyday practice is questionable. Clinicians are familiar with

topographic indices such as simk, SAI and SRI, however the introduction of additional indices -even incorporated in software with automatic calculations- is probably not easily adaptable for clinical use. *Bogan et al.* (1991) also studied the topographic patterns seen after radial keratotomy in 32 corneas and compared these results with 47 normal corneas. They found that the majority of post-radial keratotomy corneas (59%), exhibited a polygonal pattern not seen in normal corneas, whereas the rest of the corneas could be classified in one of the five patterns seen in normal corneas. The authors in their topographic classification used a combination of the objective criteria used in their normal population study, as well as criteria based on the corneal shape configuration. *Hersh et al.* (1995) attempted to define qualitative patterns of corneal topography seen after excimer laser photorefractive keratectomy (PRK). Seven topographic patterns were defined. At one year, 58.6% of corneas showed a homogeneous topography, 17.7% showed a toric-with-axis configuration, 2.8% showed a toric-against-axis configuration, 13.8% showed irregular topography, 2.8% showed a keyhole/semicircular pattern, and 4.4% showed focal topographic variants. Apart from an abstract (ARVO poster presentation) by *Tripoli et al.* (1990) there are no published studies on topographic classifications for post-PKP corneas.
As the current study has shown, the classifications for normal, post-RK and post-PRK corneas are inadequate for the great variability of topographic patterns with irregular astigmatism seen after penetrating keratoplasty. The qualitative classification proposed here, covers the great heterogeneity of the computer generated maps seen after PKP. The shape of a post-PKP cornea is invariably different to the prolate shape seen in normal corneas. A prolate shape was found in 100% of normal corneas (*Bogan et al,* 1990), but in only 3% of corneas following RK (*Bogan et al,* 1991). In the present study, of the 85 videokeratographs reviewed at the 12-month follow up visit, an equal percentage (21.1%) of prolate and oblate shape corneas were seen, with the mixed prolate/oblate shape configuration presenting more often (57.5% of cases) [Table

3.9]. *Tripoli et al.* (1990) in their abstract on 45 post-PKP corneas, also cite an equal percentage of prolate and oblate shapes (31%). The comparison with results of previous series of qualitative analysis of corneal topography is quite difficult, mainly because of the lack of generally accepted criteria for classification. There is clearly a need for establishment of such criteria, which should apply to both normal and pathological corneas. In the current study the absolute scale was used for the classification, but this is not a point of general agreement. *Bogan et al.* (1990 and 1991), in their classifications have used the normalised scale, whereas *Hersh et al.* (1995) used colour bins of 0.5 D for their analysis. It is this author's view that any attempted qualitative classification should be based on the absolute scale. The normalised scale tends to overemphasise abnormalities by providing details which may not be clinically significant, as each colour may represent an interval as small as 0.2 D [Figure 3.8]. It is suggested that a 1.5 D interval scale - such as the absolute scale- provides the best combination of sensitivity and the widest range of coverage of powers that are found on corneas after surgery, and is adequate for recognising pathology (*Wilson et al*, 1993). A single consistent scale with standardised colours should also be used by a classification scheme that could be used by different observers to monitor changes over time. Normalised scales with lower diopter intervals should only be used as adjuvants to the absolute scale. Additionally, very recently *Rabinowitz et al.* (1996) on his classification of normal corneas, has shown that pattern analysis in the absolute scale can show differences that are not obvious with the normalised scale.

In the scheme proposed here, objective criteria were used to facilitate classification. In previous studies, it is quite common to find different definitions of "irregular astigmatism", by various investigators. *Bogan et al.* (1990) defined as irregular any pattern that could not be identified as round, oval or bow-tie

TABLE 3.9 : Comparison of the topographic patterns observed in different conditions.

	Bogan et al, 1990	*Rabinowitz et al,* 1996	*Bogan et al,* 1991	*Hersh et al,* 1995	*Current study*
Study population	Normals	Normals	Post-RK	Post-PRK (12m.)	Post-PKP (12m.)
Cross sectional shape					
Prolate	100%		3%	-	21.1%
Oblate	-		79%	98.4%	21.1%
Mixed prolate/oblate	-		18%	1.6%	57.5%
Pattern					
Round	22.6%	20.8%	6%		-
Oval	20.8%	25.1%	-		3.5%
Irregular	7.1%	5.9%	6%	13.8%*	71.8%
SBT	17.5%	21.5%	16%		7%
ABT	32.1%	7.4%	6%		12.9%
Polygonal	-	-	63%		-
Other	-	19.3%	3%		4.8%

* other groups, defined by the authors as : homogenous, toric-with-axis, toric-against-axis, keyhole/semicircular, focal topographic variants account for the rest of the observed patterns.

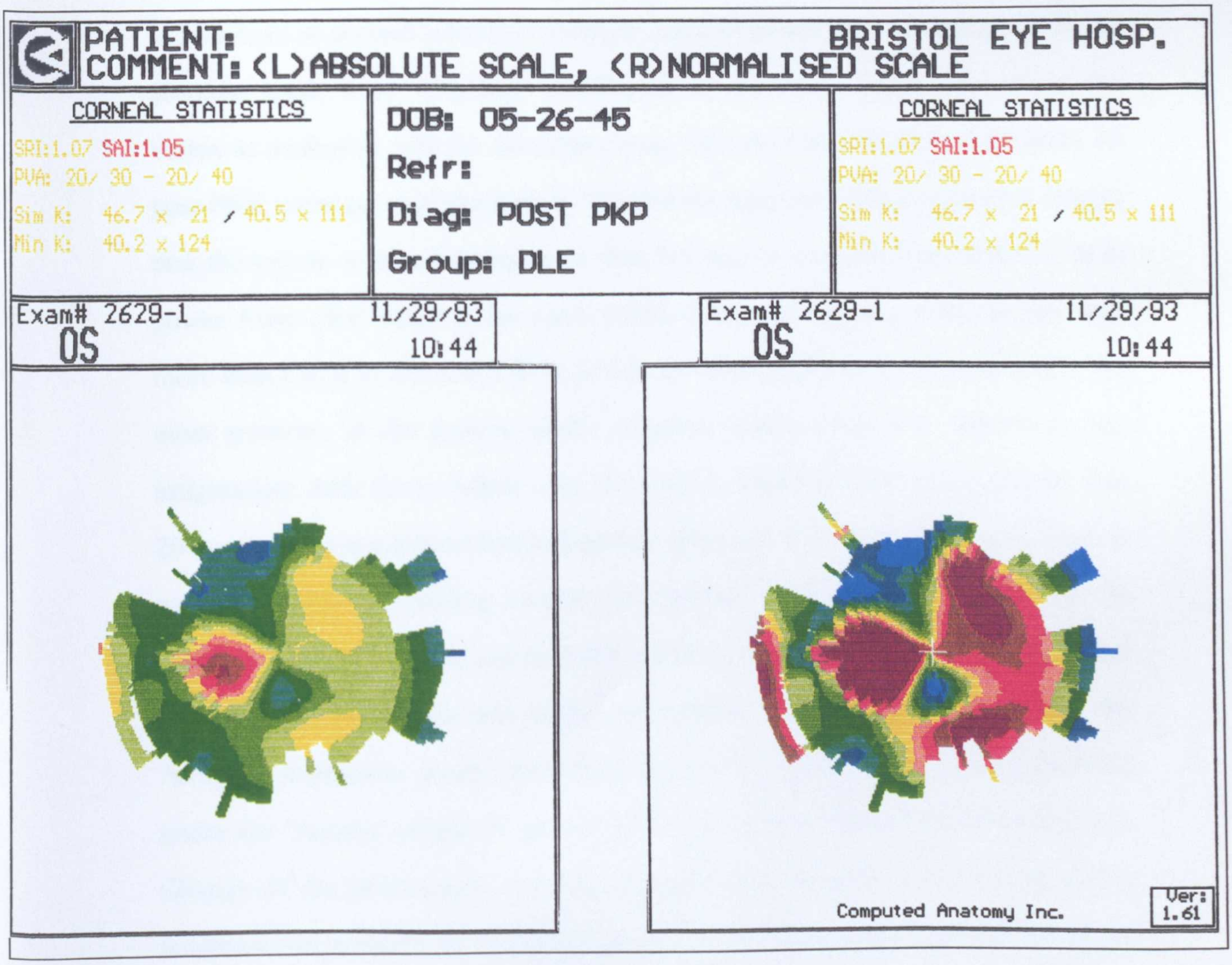


Figure 3.9 : Example of a topographic map which can be classified differently according to the scale used.

A (left) : a topographic map using the absolute scale, is classified as LS pattern.

B (right) : the same videokeratography, processed with the normalised scale. This time the topographic map is classified as PABT pattern.

according to their criteria. *Wilson et al.* (1993), subjectively determined irregular astigmatism as present whenever three or more of power interval colours with the absolute scale, were irregularly distributed on the map within 1.5 mm of the vertex as measured with the movable cursor. *Hersh et al.* (1995) in their study on post-PRK corneas, characterised as "irregularly irregular" the topographic images that showed an area measuring more than 0.5 mm in size and more than 0.5 D in power from other areas at the same radius from the optical centre, or one area more than 1 mm in size and 1 D in power not conforming to the criteria set for the other patterns. In the present study, irregular astigmatism was defined as any astigmatism with the principle axes forming an angle to each other greater than 20°, and this was subclassified in 8 distinct patterns, most of which are not seen in normal corneas. According to previous studies "irregular astigmatism" can be found in 6-7% of normal and post-RK corneas, and in 13.8% of post-PRK cases [Table 3.9]. In the current study topographic patterns classified under the "irregular astigmatic group" were seen about twice as often as patterns classified under the "regular astigmatic group" (59% vs. 30% of the 353 maps examined). Change of the percentages over the postoperative period was observed, with a tendency for increase of the irregular patterns and conversely decrease of the regular patterns over time (39%, 35%, 23.5% for the regular topographic patterns; 61%, 63%, 72% for the irregular patterns, for the 3, 6, 12 months post-PKP intervals respectively) [Figure 3.8]. This is a result of the healing process and postoperative suture manipulation (selective suture removal, single running suture adjustment).

Twelve distinct topographic patterns for post-PKP corneas were identified. Although some of the irregular patterns, such as the triple and the horseshoe pattern have not been described in conditions other than post-PKP, other irregular topographic patterns can be seen in different pathological conditions. Images such as the PI [Figure 3.5A] and mixed pattern [Figure 3.5B,D] can also be associated with conditions such as pterygium, peripheral gutter, localised thinning (*O'Brart et* *al*, 1995) or pellucid marginal corneal degeneration and keratoglobus (*Karabatsas & Cook*, 1996). The classification chart suggests that some patterns may arise from others (indicated by the arrows in figure 3.1), whereas other patterns such as the triple, LS and unclassified do not belong in any kind of continuum. A suggestion of continuity in the patterns seen in normal corneas has been advocated (*Bogan et al*, 1990). The spectrum of post-PKP topographic patterns may be explained by a number of factors that theoretically could influence changes over time. Variations in corneal hydration post-operatively, changes in the steepening and flattening forces that develop at the graft-host interface secondary to the epithelial and stromal wound healing and remodelling, or the effect of sutures, can all be related to topographic changes. In particular, bow-tie patterns might indicate meridional differences in wound healing. *O'Brart et al.* (1995) have proposed an explanation for the topographic changes seen in various pathological conditions due to disruption of corneal stroma. Loss of peripheral corneal stroma usually produces flattening of the central cornea in the perpendicular meridian, also affecting areas of 'normal' cornea, quite distant from the site of the original pathology. When peripheral gutters extend circumferentially, then the vector forces are complicated. Forces acting at the extremities of the gutter produce an 'arching' effect to the normal 'bow-tie' pattern. A similar mechanism, not by disruption of the corneal stroma, but by forces acting at the corneal stroma, especially at the graft/host interface secondary to the healing response, might explain the progression of a symmetric or asymmetric bowtie pattern [Figures 3.4A,B] to an irregular pattern [Figures 3.5A,B] in post-PKP corneas. External compression on the other hand (in these cases by tight sutures) causes flattening of the globe directly under the area of compression, with steepening of the curvature adjacent to the area of compression (*van Rij & Waring*, 1984). When sutures are present in different locations, then the resulting vector forces affect the topographic pattern.

Of the variables that were looked at in this study, non-keratoconic eyes were found to show consistently (at least for the 6 to 12 months postoperative period) significantly more irregular astigmatic patterns (in particular LS) than keratoconic eyes. Conversely, regular astigmatic patterns (in particular the OABT pattern) was more often seen in keratoconic patients. Whilst suture manipulations were similarly performed in both groups, these differences may reflect a variability in wound healing between keratoconic and non-keratoconic patients, or even differences in fundamental tissue characteristics such as tissue compressibility. Regular astigmatic patterns were also found to correlate with a greater amounts of topographic astigmatism. Significantly higher topographic astigmatism (simk) values ($P=0.05$) were recorded in regular astigmatic patterns (5.09 ± 4.12 D) than in irregular astigmatic patterns (3.70 ± 2.15 D), at 12 months following keratoplasty. This finding is in accordance with studies showing that keratoconic patients had higher astigmatism after keratoplasty (*Troutman & Gaster,* 1980; *Wilson & Bourne,* 1989; *Kirkness et al,* 1991). *Bogan et al.* (1990) in their study on normal corneas, did not detect a statistically significant difference in astigmatism between corneas with round and oval patterns, but there was clinically meaningful increase in astigmatism in corneas with symmetric or asymmetric bow-tie patterns. In the classification proposed here, bow-tie patterns are classified as regular astigmatism, therefore it seems that regular astigmatic patterns whether seen on normal or post-PKP corneas, are associated with an increased amount of astigmatism.

Of the investigated quantitative indices, no association was found between SRI and pooled regular or irregular astigmatic groups. SRI was designed statistically to allow for local corneal power fluctuations along each semimeridian (*Wilson & Klyce,* 1991b). The SRI algorithms determine as irregularity the difference in power gradient between successive mire pairs. Therefore, regularity is defined differently to our classification where the angle α [Figure 3.2] was considered. Moreover SRI algorithms compute data only from the central 10 photokeratoscope mires. Only the central 3 to 4 mm of the cornea are therefore analysed (to approximate the entrance pupil). However, the qualitative classification proposed here, is based upon interpretation of topographic maps covering the whole donor corneal surface. Conclusively, patterns such as LS, horseshoe, SF or mixed could be classified as irregular, but on the other hand may show low SRI values because of a relatively homogenous central corneal power. In fact, low mean SRI values were observed with the horseshoe, mixed and SF patterns (0.87, 0.88, 1.11 respectively), lower than the average SRI of the pooled regular astigmatic group (1.24).

Significantly lower SAI values were observed with regular astigmatic patterns than with irregular patterns. Furthermore, topographic maps classified as asymmetric (PABT, OABT), showed higher SAI value than symmetric patterns (PSBT, OSBT). This index appeared to be more useful than SRI in distinguishing between regular / irregular and symmetric / asymmetric patterns and it could be used as an additional aid for the qualitative classification of ambiguous cases. The SAI index by summating the absolute differences between dioptric power of symmetric points in opposite semi-meridians, checks both radial symmetry as well as regularity of a corneal surface. By definition, the index would be zero both for a perfect sphere as well as for any surface with a power that is radially symmetrical, but also for a surface with perfectly spherocylindrical regular corneal cylinder (*Dingeldein et al,* 1989). Such a surface according to our criteria ($\alpha<20^{o}$) would be classified as regular. It follows that the more regular surfaces will exhibit lower SAI values, something confirmed by the findings of the present study.

The proposed classification of post-PKP topographic patterns, may have potential clinical applications such as : *(a)* facilitating communication among clinicians and investigators by utilising a standardised classification system for both normal and pathological corneas; *(b)* observing changes over time in a standardised manner; *(c)* relating certain topographic patterns to a specific suturing technique or diagnosis. If such association is established, then suggesting certain surgical strategies (suturing techniques, removal of sutures, suture adjustment) that could avoid less desirable patterns. Some aspects of this question are examined in the next chapter 4; *(d)* screening for and planning refractive surgery in post-PKP corneas as well as monitoring the postoperative outcome would, a topic discussed in chapter 5.

3.6. Conclusions

In summary, the following conclusions arise from the present study:

1. The proposed classification showed a high interobserver agreement, a pre-requisite for clinical use.

2. Twelve distinct topographic patterns after PKP were identifiable and some of them may form a continuum.

3. In postkeratoplasty corneas, the incidence of irregular astigmatism is about double that of regular astigmatism (59% vs. 30% respectively). Furthermore prolate and oblate patterns are seen in equal proportions (21%), with mixed prolate/oblate shape seen in 57.5% of the cases.

4. The topographic patterns showed a change over time; a decrease in the regular astigmatic patterns, with a corresponding increase in the irregular astigmatic patterns.

5. An association of keratoconic eyes with regular astigmatism (in particular OABT pattern) and non-keratoconic eyes with irregular astigmatism (in particular LS pattern) was also seen.

6. Regular astigmatic patterns were associated with significantly higher astigmatism measurements.

7. The SRI index failed to demonstrate differences between regular and irregular astigmatic patterns, but the SAI index was significantly lower in the regular astigmatic patterns.

CHAPTER 4

A PROSPECTIVE RANDOMISED STUDY OF INDUCED ASTIGMATISM RELATED TO SUTURING TECHNIQUES DURING PENETRATING KERATOPLASTY

4.1. Introduction

Although extreme astigmatism prevents or delays visual recovery, successful keratoplasty can still be achieved in its presence. An improvement in the patient's field of vision, contrast sensitivity, even pain relief in certain conditions are considered as reasonable surgical outcomes. It is also the fact that other features such as spherical ametropia in absolute terms or relative to the fellow eye, must be considered in individual circumstances. Such targets are in no way contrary to the efforts that surgeons should put at all times, to reduce astigmatism to a minimum. As discussed in general introduction (chapter 1), one of the main factors contributing to post-keratoplasty astigmatism is the suture technique employed by the surgeon. A number of different suturing techniques have been proposed to reduce astigmatism after PKP. In 1977 *McNeill & Kaufman* reported the use of double running sutures (10/0 and 11/0 nylon). Removal of one continuous suture (usually the 10/0 after 3-6 months) however, is followed by an unpredictable shift in astigmatism (*Lin et al,* 1990a), although *Musch et al.* (1988) have reported that the change in cylinder following removal of the 10/0 continuous suture is not significant. In 1982 *Stainer et al.* popularised the use of eight interrupted 10/0 nylon sutures followed by an eight-bite overlay continuous 11/0 nylon suture. The interrupted sutures could then be selectively removed during the postoperative period as directed by the refraction or keratometric readings. This technique was shown to decrease astigmatism and to improve visual acuity. *Binder,* later published two separate series of patients (1985a, 1988) which supported Stainer's findings. Several reasons can limit the effect of selective suture removal. Multiple adjacent sutures cannot be removed in the very early postoperative period because of the risk of wound dehiscence. Furthermore, suture removal results in relaxation of tension, but cannot induce an increase or re-distribution of tension. To improve on these deficiencies, *McNeill & Wessels* (1989) described the use of a single continuous running suture allied to early post-operative suture redistribution of tension. The suture is adjusted at the slit lamp as directed by refraction and/or keratometry. This retrospective study demonstrated a significant reduction in cylinder. Later series by *Lin et al.* (1990b), *Van Meter et al.* (1991), *Nabors et al.* (1991) and *Hope-Ross et al.* (1993) have confirmed those results. The lack of large prospective randomised studies however, comparing the technique of the single adjustable suture to other known suturing methods does not permit a direct comparison of the effect of each technique on the surgically induced astigmatism. In order to specifically test the hypothesis that a "new" technique is more effective in reducing astigmatism than an alternative treatment, a prospective randomised clinical trial is required (*Ferris,* 1986).

4.2. Objectives of the study

The following study was designed to evaluate the single continuous adjustable suture (SCAS) in PKP, and whether this compares favourably to the interrupted and continuous (ICS) suturing technique in the amount of induced astigmatism during the first postoperative year. The proposed study was designed to contribute to our knowledge and understanding of the problem of post-PKP astigmatism in a prospective and comparative manner with the aid of computer assisted videokeratography.

The main objectives of the study were to :

1. determine the induced changes in power, axis and topographic pattern of astigmatism, associated with the two different suture techniques at defined intervals during the first postoperative year.
2. assess the general behaviour of the single running 10/0 nylon suture in PKP.
3. assess the efficacy of postoperative adjustment of a running 10/0 nylon suture in managing post-PKP astigmatism.
4. evaluate the effect of selective interrupted suture removal in the reduction of astigmatism.

A secondary question to be answered by the study, was the safety of the two techniques (identification of complication rates).

The astigmatic goal was a value of less than 3.5 D, as in other similar studies (*Bertram et al,* 1990); to achieve this, CAVK was employed in every case.

4.3. Design of the investigation / Subjects and methods

This study was a mono-centre prospective randomised study. The study population consisted of patients undergoing PKP at the Bristol Eye Hospital, under the care of the hospital's two corneal teams. Patients were enrolled between October 1992 and October 1994, and their follow-up was completed by October 1995. The research protocol had the United Bristol Healthcare Trust's Ethical Committee approval.

4.3.1. Patient selection

Patients were eligible for the study entry if they had a minimum age of 18 years and were undergoing corneal grafting for visual indications. Patients receiving combined corneal grafting with cataract extraction, with or without IOL implantation were also included. The exclusion criteria for the study were : (1) patients undergoing tectonic, therapeutic or cosmetic corneal grafts, (2) any patient deemed unsuitable to receive one of the prescribed surgical techniques as described below. These included acute corneal perforations, severely inflamed or vascularised eyes that the surgeons thought preoperatively were not suitable for either, and they should have interrupted sutures only, (3) patients unable to cooperate for the postoperative follow up, especially for slit-lamp suture removal or for the acquisition of the refractive, keratometric and topographic data (usually mentally handicapped persons).

A total of 129 consecutive eyes planned for PKP were screened, 98 of which met eligibility criteria and were initially enrolled. Written informed consent was obtained from each patient before the operation. An initial examination was performed before randomisation. Eligible patients were immediately randomly assigned according to a random numbers table, to one of the two groups : ICS or SCAS. Because of the controlled nature of the trial, if within the study period a patient had to be operated on both eyes, then one surgical technique (assigned by randomisation) was performed on one eye, and the other surgical technique on the fellow eye, as has been suggested by *Waring* (1987b).

Three initially enrolled cases were excluded from the analysis; two patients for primary graft failure within the first postoperative week (their second procedure included however), and one patient for extensive loosening of the suture within the first week (repeat graft with interrupted only sutures). Of the remaining 95 cases, 51 were randomly assigned to the combined running and interrupted suture group (ICS) and 44 to the single continuous adjustable suturing group (SCAS).

4.3.2. Training of surgeons

The 6 surgeons involved in the study, operated on a random basis. They all had formal training in corneal and refractive surgery, in addition to their general ophthalmic training (either consultants ophthalmologists undertaking mainly corneal work, or corneal fellows/senior registrars under the supervision of a more experienced surgeon). Throughout the study, the performed operations were monitored by the author, to insure adherence to protocol. As the SCAS technique had not been performed at Bristol Eye Hospital before this study, early pilot cases performed during the months of August and September 1992 with the technique, were omitted from the database so that individual variation in rate of learning and early mistakes did not cloud the effect of the surgery when properly performed.

4.3.3. Tissue supply

All donor corneas used in this investigation, were stored by the Bristol Corneal Transplant Service eye bank in organ culture (Eagle's medium) at 34^{o} C for up to 4 weeks and were subject to quality assessment and allocation procedures. The corneal endothelium was examined prior to transplantation to ensure adequate cell density and morphology and was considered not suitable if $< 2{,}000$ cells/mm^2.

4.3.4. Surgical techniques

Surgery was performed using either general or local anaesthesia under the operating microscope. Betadine solution was used for the periocular preparation.

All eyes were stabilised with a four-point scleral support McNeill-Goldmann ring sutured to the episclera with four 4/0 Dacron sutures at the 2, 4, 8 and 10 o'clock positions. Cauterisation was used at the apex of the cone and around it in some advanced keratoconic patients, to reduce a significant cone to a more regular corneal shape prior to trephination and reduce the astigmatism, as suggested by *Hatch* (1980). Cauterisation also makes trephination easier. The visual axis was marked by using a Sinskey intraocular lens hook with the tip inked with a sterile marking pen, or the tip of the marking pen itself to simply achieve a small dent in the epithelium by gentle depression. Donor corneas were cut with the Weis punch, a mechanical punch with little play and consistent cut, after the corneo-scleral discs were placed epithelium side down, with a drop of storage medium on a Teflon block and centred for alignment. Storage medium was always dispatched for bacteriological testing. After the application of an inked 12-point radial keratotomy marker, host corneas were cut with the Hessburg-Barron suction trephine (Jedmed, St Louis, MO, USA) with its cross hairs centred on the previously marked visual axis. This is a disposable suction trephine for selected partial or penetrating keratoplasty, described by *Hessburg & Barron* (1980). The cutting of the host's button was completed with diamond knife or scissors and the wound checked for abnormalities such as shelving of the inferior stroma. The recipient bed ranged from 6.75 to 8.00 mm in diameter and in all cases donor grafts 0.25 mm larger than the host trephine were used.

Some patients had additional surgical procedures such as extracapsular cataract extraction, IOL removal, IOL insertion, gonioplasty, iridoplasty, and anterior vitrectomy [Table 4.1]. In all cases where IOL was exchanged, or in cases where the posterior capsular support was absent, the method of iris fixation IOL was used. This was oriented vertically behind the iris. Fixation was achieved with two double-armed 10-0 polypropylene sutures (Prolene) at the peripheral iris. The two types of IOL used in the series, were either a one-piece all PMMA 7 mm diameter optic IOL (PCUB-26, Surgidev) or a three piece IOL (UV 20-20, Surgidev).

Upon completion of donor punch and recipient trephination, Healon was applied to the anterior chamber and the donor button was placed in the recipient opening with the use of Paton's spatula. The button was then sutured into position with four cardinal 10-0 nylon sutures at 3, 6, 9 and 12 o'clock positions with the use of Pollack's forceps and a compound curved needle. Traumatisation of the edges of both graft and recipient cornea was carefully avoided.

The donor button was then sutured into position with one of two closure techniques according to the assigned treatment group.

a) *Interrupted & Continuous suturing* (ICS) [Figure 4.1]

Additional interrupted sutures on each remaining clock hour were placed for a total of 12 interrupted 10/0 (22 μ diameter) nylon sutures. The 12 evenly spaced marks of the radial keratotomy marker guide regular suture placement. Sutures were placed at the level of Descemet's or through and through, extending about 1.5 mm into donor and recipient tissue. These sutures were tied relatively tight for good primary wound closure. The aim is to tie all sutures with equal tension, and all sutures judged too loose, too tight or non-radial by visual inspection under the microscope, were removed and replaced intraoperatively. The knots of the interrupted sutures were then rotated and buried into the recipient cornea with a Tennant tying forceps. Following this, the running 11/0 nylon suture (15 μ diameter) was placed in a clockwise fashion, with a radial bite on each half clock hour, and at between 1/2 and 2/3 tissue depth. At completion of the 12 bites, the suture was knotted with only enough tension to approximate the tissues. Finally the wound was checked for aqueous leak on the operative table.

b) *Suturing with the single running technique* (SCAS) [Figure 4.2]

After placement of the four interrupted 10/0 radial graft alignment sutures, a single radial 24 bite 10/0 nylon suture was used to secure the donor button. The positioning of the sutures bites was guided by the 12 radial keratotomy marks. The cardinal sutures were removed and the IOP was raised to normal. The suture was then carefully tightened and tied with just enough tension to prevent perioperatively leakage. The knot was buried in the recipient stroma. The first adjustment was actually made perioperatively based on the corneal reflection from a safety pin acting as a basic hand-held keratoscope. In some cases also an intraoperative surgical keratometer was also used if the surgeon felt this was required. When a wound leak was present after inflation of the anterior chamber, additional 10/0 nylon interrupted sutures were placed. These were removed in the early postoperative course, so only the single continuous suture was left.

4.3.5. Patient postoperative care and follow up protocol

Topical corticosteroids and antibiotics were administered in tapering dosages following surgery. The topical antibiotics were usually stopped after about a month, but the topical steroid treatment continued for at least the first 6 months. Patients were treated with topical cycloplegics, β blockers, systemic carbonic anhydrase inhibitors, acyclovir, oral immunosuppression, or anti-acanthamoeba topical medications (PHMB, Propamidine isethionate), as clinically indicated.

To avoid variable periods of follow-up with life table methods, all patients were prospectively followed for one year. The minimum number of postoperative visits were at 1 day, 1 week, 1, 3, 6, 9 and 12 months, whereas extra visits were included as necessary according to the physicians judgement. A time 'window' of two weeks was established within a visit and accepted as providing the necessary data on the patient's status (*Seigel,* 1985).

4.3.6. Clinical examination: Conditions, techniques and instruments

Standardised conditions for postoperative clinical examination were assured for every patient. Examination room (lighting conditions, Snellen chart) and equipment were identical in all cases. At each postoperative visit, uncorrected and spectacle corrected visual acuity, slit lamp biomicroscopy and retinal examination were performed. Manifest refraction with the fogging technique and the use of the cross cylinder (retinoscopy with subjective refinement) was also recorded on every visit. Refraction was verified by a second examiner when necessary, and astigmatism was always expressed in terms of positive cylinder. Three keratometric measurements and videokeratographic images were also obtained from each eye at every visit. The type of the instruments used (10 SL/O Zeiss keratometer, TMS-1), their mode of operation and calibration have been described in detail in the previous chapters 2 and 3. No form of artificial tears was used to improve quality of mires.

The presence or absence of the following complications were also recorded on a standardised data sheet at each visit : infiltration, infection, broken suture, epithelial defect, neovascularisation, allograft reaction, graft failure, tight suture, loose suture, wound leak, cheesewiring, dehiscence, exposed knot.

4.3.7. Principles of the selective suture removal technique

During this study, corneal topography was the employed method to identify tight sutures. One to six interrupted sutures were selectively removed at a time, from the steep semimeridian(s) in order to reduce astigmatism, according to the topographic picture ("hot" colours), not earlier than the tenth postoperative week. The 10 weeks visit is considered a safe time interval from surgery and this practice has been followed by the two corneal firms at Bristol Eye Hospital in manipulating sutures on post-PKP patients. In eyes where corneal topography showed a significant astigmatism but there was little manifest astigmatism on refraction or keratometric astigmatism (less than 3.5 D), the sutures were left in place until a subsequent visit when more reliable data could be obtained and corneal topography matched the refractive astigmatism. Once the tight sutures were identified, using topical anaesthesia at the slit lamp, they were cut with the sharp edge of a disposable 22-gauge hypodermic needle and removed with a tying forceps on a jerking centrifugal direction. According to the case, a number varying between 1 to 3 sutures per semimeridian, had to be removed [Figure 4.3]. Depending on the pattern of astigmatism, the semimeridians were not often on the same axis. Interrupted sutures were also removed if they broke or loosened excessively. The continuous 11/0 suture was left in place for as long as it would take to biodegrade, and it was only removed if it spontaneously loosened or broken. It could also be removed after the first year in those eyes that excessive astigmatism could not be controlled by selective suture removal. The location and reason for removal of all sutures was noted on the protocol sheet. Appropriate topical antibiotic and steroid cover was given to prevent any infections or allograft rejections that may be triggered by suture manipulation.

4.3.8. Suture adjustment technique

Suture adjustment was undertaken when the topographic astigmatism (simk) was greater than 3.5 D, with the absolute scale topographic map as a guide. Suture adjustment could start as early as possible following surgery, provided that a reliable topographic map could be obtained. The technique of postoperative suture adjustment as was initially described by *McNeill & Wessels* (1989) [Figure 4.4] involves rotating the suture from the area of flat meridian ('cool' topographic colours) and proceeding loosening towards the area of the steep meridian ('warm' topographic colours) [Figure 4.5]. The tension of the suture is redistributed by gentle rotation with forceps on a loop to loop basis. The slack from each tightened loop is passed to the next loop. The straight tying forceps (Birk's), or the McPherson's forceps were used as a suture adjuster according to the surgeon's preference; with the latter it was felt that it was easier to pass the platforms safely under each loop and then pull them in the direction of the loop. The great majority of the cases presented in this study were adjusted with topical anaesthesia under the operative microscope [Figure 4.6], but some of the later cases were performed at the slit-lamp as we became more familiar with the technique.

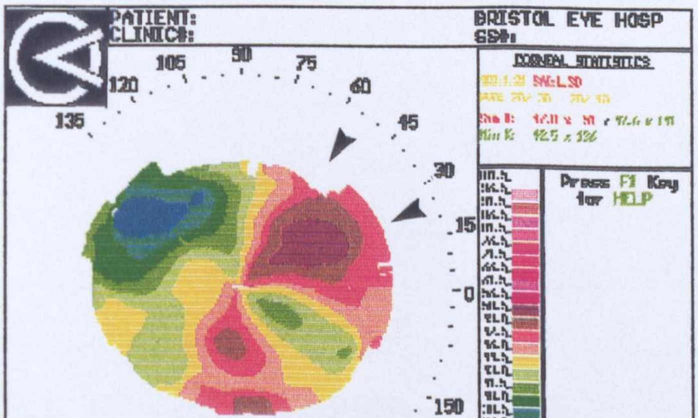
4.3.9. Data management

Each patient had an enrolment spreadsheet in their notes. Although the notes were always available for reference, data forms were stored separately from routine clinical records. Results were entered into a computer spreadsheet program (Excel Microsoft, Seattle, WA).

Figure 4.1 : Photograph of an eye operated with the interrupted (12 x 10/0) and continuous (11/0) suturing technique (ICS).

Figure 4.2 : Photograph of a corneal graft sutured in place with a single continuous 10/0 nylon suture (SCAS).

Figure 4.3 : Topographic map (PI pattern) of an eye 12 weeks following PKP. Arrows indicate position and number of interrupted sutures to be removed in order to reduce the postoperative astigmatism.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SMOOTH = 1
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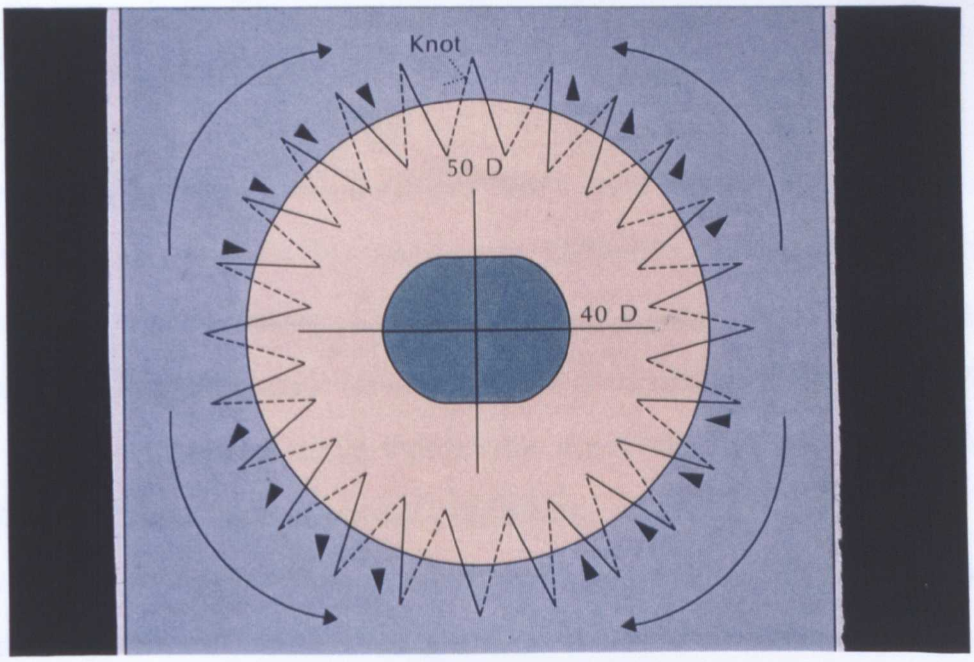
Exam# 3041
Photo# 1

Figure 4.4 : During the adjustment procedure, the 10/0 suture is grasped with tying forceps at the flat semimeridian and tightened, so that it can be loosened at the steeper semimeridians by redistribution of the tension (adapted from *McNeill & Wessels,* 1989)

Figure 4.5 : This is an example of suture adjustment plan based on the absolute scale topographic map. Adjustment should start from the 'cool' colour areas (9 and 3 o'clock positions), proceeding towards the 'warm' colour areas.

Figure 4.6 : Surgeon adjusting the single continuous 10/0 nylon suture under the operating microscope. The adjustment planning drawn out on the topographic map, is affixed to the microscope in full view of the surgeon so it can be used as a reference source. In the case shown here a keratoscope attached to the microscope was used to judge qualitatively adequate adjustment. This requires frequent instillation of fluid to visualise the mires; it was found not to be necessary after sufficient experience was achieved following the first cases.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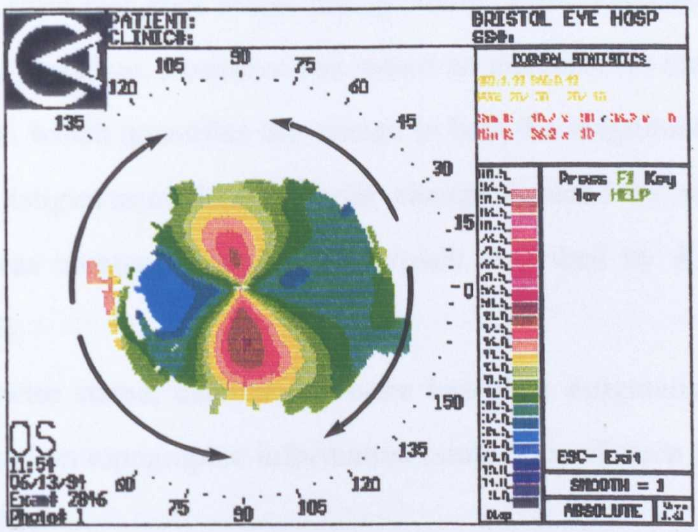
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4.3.10. Outcome evaluation

Calculation of astigmatism change

Corneal astigmatism was measured with both keratometry and CAVK. Keratometric astigmatism was taken as the difference between the steep and flat central keratometric readings; as topographic astigmatism was considered the simk value. In addition, refractive astigmatism was obtained by the subjective cylinder. The proposed classification of topographic maps (chapter 3) was also used for qualitative interpretation of corneal astigmatism.

The change in astigmatism was calculated by: (1) the subtraction method: subtracting the net corneal astigmatism at the examination before suture manipulation from that after suture manipulation. Thus, a negative value means a decrease in astigmatism, a positive one means an increase; (2) the vectorial change in astigmatism which quantifies the change in both the magnitude and direction of the induced astigmatism. The vectorial change induced by suture removal or adjustment was measured using the approach described by *Kaye et al.* (1992) [Appendix V].

Unless otherwise stated, calculations were based on astigmatic data (magnitude and axis) based on topographic information (simk, axis of steep meridian).

Optical stability

Optical stability was defined as a reduction in astigmatism to 3.5 D or less, or until further suture manipulation was not possible (i.e. no tight suture remaining in steep axis).

Patients analysed

Baseline characteristics are reported for the 95 eyes studied. Outcome is reported for 85 eyes that completed the final follow-up visit at 12 months. Ten patients did not have final follow-up data: five deceased (three in the ICS group, two in the SCAS group), two had rejected (both in the SCAS group), two had to be regrafted (both of the SCAS group), and one (ICS group) moved elsewhere. Data from these patients are included however in the calculations up to their last visit. On some occasions, keratometric readings were missing during the follow up period from patients who had very irregular, unreliable keratometric readings.

Visual acuity is dependent on different variables not directly related to the surgical technique and postoperative management. Additionally, the potential visual outcome and the preoperative fundus condition was not considered in the inclusion criteria of the study. For this reason visual outcome was not compared between the two treatment groups.

4.3.11. Statistical methods

Sample size considerations

To determine sample size, the primary end point used to define clinically significant difference in astigmatism at final follow up between the two groups was 2.00 D or better. To have a 90% chance of detecting such a true difference (with a SD of 2.00 D) at the 5% level of significance, the sample size required was calculated to be 42 patients for both groups (*Florey,* 1993). Given the sample size of 95 patients that were studied, the difference between the two groups of treatment that could be detected with 90% power would be as small as 0.95 D.

Treatment group comparisons

Descriptive statistics including 90% confidence intervals were calculated. Independent sample, two-tailed Student's *t* test were used, with logarithmic transformations to account for any departures from normality, to check for differences. The influence of the suturing technique on astigmatism was analysed with a two way analysis of variance (ANOVA) with repeated measures. *Time* effects represent changes from baseline during the study. *Treatment* effects represent a difference in response between the two groups (SCAS vs. ICS). *Treatment/time* interaction indicates the way that astigmatism changes over time. Data were tested with the Mauchly sphericity test to determine normal distribution. Non-normal data were corrected by Greenhouse-Geisser factor. Where significant treatment-time interactions were indicated, the exact level of significance at individual time points was calculated using a paired *t*-test, using the variance term for the interaction from ANOVA and a Bonferroni correction for multiple testing. Statistics are presented as F-ratio and probability. To determine demographic or clinical factors associated with the amount of astigmatism, single factor ANOVA was used among the different categories of factors. Correlations were performed with Spearman's rank correlation and simple linear regression analysis. Categorical variables (e.g., baseline characteristics, topographic patterns, complications) were compared among the two treatment groups using Fisher's exact chi-square test. Significance was accepted if the p value was < 0.05 for all statistical tests. Data were statistically analysed personally with the SPSS statistical package on an IBM compatible computer.

4.4. Results

4.4.1. Study population

Table 4.2 shows the demographic characteristics of the 95 cases operated in this study and Table 4.3 shows the preoperative indications for surgery. No significant differences in sex or eye (right or left) were present at the baseline between the two groups. Patient age ranged from 18 to 89 with a mean age of 57.1 years in patients who underwent IC suture wound closure and 50.5 years in patients who underwent SCAS wound closure. However, significantly more patients at the above 65 y.o age group were operated with the SCAS ($p < 0.01$). There was no significant difference between the other age groups. Randomisation produced comparable groups at baseline ($p > 0.12$ for all diagnoses). The most common preoperative diagnosis was keratoconus for both groups [18 of the 51 eyes (35.3%) in the ICS group as compared to 20 of the 44 eyes (45.4%) in the SCAS group], followed by Fuchs' endothelial dystrophy [10/51 (19.6%) of the eyes in the ICS group and 4/44 (9%) eyes in the SCAS group]. Re-examination of the treatment allocation after the completion of the study, revealed that adherence to the suturing technique randomisation schedule was excellent. Only one of the 95 (1.05%) subjects received a suturing technique other than that assigned by the study randomisation (ICS instead of SCAS). Six patients had bilateral surgery, but not at the same time.

4.4.2. Operative characteristics

All 95 cases in the study were operated on with a 0.25 mm trephine diameter disparity between host and donor button. The trephine sizes used for the recipient beds ranged from 6.75 to 8.00 mm. They were distributed as follows : a 6.75 mm trephine was used in one case; a 7.00 mm trephine in 43 cases; a 7.50 mm in 43 cases; 7.75 mm in one case, whereas in 7 cases the 8.00 mm trephine was used. For the donor corneas trephination size ranged from 7.0 to 8.25 mm. In all but 3 cases (all in the ICS group), surgery was performed under general anaesthesia. Of the 6 surgeons involved in the study, not all were present with the same frequency. Four surgeons have operated on 80/95 cases (84.2%). Randomisation also assured that no surgeon operated only on one technique.

4.4.3. Follow up data

The overall follow up rates were 98%, 94%, 95% and 91% at 3, 6, 9, and 12 months respectively. Apart from the patients missing appointments for reasons described in the 4.3.10 section, no patient was lost to follow-up.

4.4.4. Timing of suture manipulation

Interrupted sutures were selectively removed as early as 10 weeks and as late as 52 weeks following PKP (mean 20.6, SD : 11.3 weeks). Running sutures were adjusted between 3 weeks and 40 weeks post-PKP (mean 13, SD : 9 weeks). The difference in time of suture manipulation between the two groups was statistically significant ($p<0.001$).

4.4.5. Number of interrupted sutures removed per visit

The results of suture removal reported here, include only sutures judged to be tight according to the topographic map. Sutures that were loose as seen on slit-lamp were also removed but are not included in the analysis of the results.

In the cases where interrupted suture removal was undertaken, the number of interrupted sutures removed per visit varied between 1 and 6. Removal of two interrupted sutures (in the same or in any meridian) was the most common procedure [Table 4.4].

4.4.6. Number of visits for suture manipulation

Selective removal of interrupted sutures at a single examination visit was carried out in a total of 75 visits (1.5 visits per patient). The patients who underwent suture adjustment incurred 55 adjustment visits over the 12-month period (1.25 visits per patient). In 6 patients (11.7%) of the ICS group and 9 patients (20.5%) of the SCAS group (p=0.19), no suture manipulation (either selective removal or adjustment) was necessary at any visit, as astigmatism was less than 3.5 D throughout the follow up period. In 16 eyes of the SCAS group (38%) only one suture adjustment was required, in 11 cases (26%) two suture adjustments, whereas in 6 eyes (14.3%) three suture adjustments were necessary.

4.4.7. Effect of suture manipulation on amount of astigmatism

The effect of both interrupted sutures removal and single continuous suture adjustment was studied. Removal of one to six interrupted sutures produced an average of 1.92 ± 3.18 D reduction in topographic astigmatism [Table 4.4]. Following suture removal, the mean astigmatism was 4.76 D (SD: 2.99 D), whereas the mean astigmatism before suture removal was 6.69 D (SD: 3.11 D). The decrease after the procedure was significant (p=0.0002). Before the manipulation of sutures, the greatest recorded corneal topographic astigmatism was 18.5 D and the minimum 1.9 D. The greatest amount of astigmatism reduction on an individual patient was 12.5 D. However, there were 13 cases (17.3%) in which astigmatism increased rather than decreased, and 14 others (18.7%) with minimal change (less than 1 D). In the remaining 48 cases (64%) a reduction in the simk astigmatism was observed [Table 4.5, Figure 4.7]. It was also found that the greatest change (3.14 ± 3.69 D) occurred when 3 sutures were cut simultaneously [Table 4.4]. These were usually at two different semimeridians. However, the range of change was wide (from 12.5 D decrease to 3.8 D increase in astigmatism). The safest method to decrease topographic astigmatism was to remove one suture. Although this method did not provide the greatest mean decrease (2.14 D), for 90% of the eyes the net change was decrease of astigmatism from -1.31 to -2.97 D [Table 4.4].

Adjustment of the running suture produced an average net reduction of 2.71 ± 4.24 D of astigmatism [Table 4.4], from 7.18 ± 3.12 D before, to 4.46 ± 3.24 D after adjustment. This difference (-3.66 to -1.76 90% change interval) was statistically significant ($p<0.0001$). The greatest net reduction on an individual patient was 6.9 D after a single suture adjustment. Moreover, the net astigmatic reduction in the SCAS group was not significantly greater than in the ICS group ($p=0.25$). Before suture adjustment the greatest recorded topographic astigmatism was 14.4 D and the minimum was 1.7 D. As with the ICS group, in 16.4% of suture adjustments astigmatism increased after the procedure, in 9% of cases the change was less than 1 D and in 74.6% of cases the astigmatism was effectively reduced [Table 4.5, Figure 4.7]. Greater than 3 D reduction of astigmatism was most likely to be seen with the suture adjustment rather than with the selective sutures removal ($p=0.05$).

4.4.8. Effect of suture manipulation on astigmatic axis

Selective removal of interrupted sutures changed the axis of the steep meridian from 0^o to 40^o in 65.3% of the cases (0-20^o in 46.6%, 21-40^o in 18.7%, 41-60^o in 16%, 61-80^o in 13.3%, 81-90^o in 5.3%). Respectively, the continuous suture adjustment changed the steep meridian axis from 0^o to 40^o in 73.7% of the cases (0-20^o in 50.9%, 21-40^o in 21.8%, 41-60^o in 11%, 61-80^o in 16.4%). The difference in shift was not significant for any of the subgroups between the two groups.

4.4.9. Vector analysis of induced astigmatism by suture manipulation

Single running suture adjustment produced greater, but not significantly, vectorial change than selective suture removal (7.40 ± 4.17 vs. 6.28 ± 4.14, $p=0.13$). Additionally, a trend was found for greater reduction with increased number of suture removal per visit. The greater the number of interrupted sutures removed, the greater was the observed vectorial change (3.81 ± 3 D for a single suture removal, 9.58 ± 3.9 D for five interrupted sutures removed at the same visit) [Table 4.4].

4.4.10. Effect of suture manipulation on topographic pattern

In 24/75 (32%) suture manipulations of the ICS group and in 12/55 (21.8%) cases of the SCAS group (p=0.342), selective suture removal or suture adjustment did not alter the topographic map classification. In 20/75 (26.7%) cases of selective suture removal and 20/55 (36.4%) cases of suture adjustment (p=0.160), the topographic map was altered, but it would still be classified under the same pooled group (regular/irregular) after the suture manipulation. A striking similar percentage of ICS eyes (41.3%) and SCAS eyes (41.8%) changed their topographic map classification group (from regular to irregular, regular to non astigmatic, irregular to non-astigmatic) after suture manipulation. The only statistically significant difference between the two groups, was the change from irregular to regular astigmatic patterns which occurred in 8/75 (10.6%) cases of selective suture removal, compared to only 1/55 (1.8%) cases of suture adjustment (p<0.001).

4.4.11. Change of topographic patterns over time

The incidence of topographic patterns for the two groups at different time intervals following the PKP, are shown in Table 4.7 and Figure 4.8. There was a significant difference (p<.001) between ICS / SCAS groups for regular/irregular patterns at the 3 months post-PKP interval, but thereafter the differences for the pooled groups (regular/irregular) were not significant. Stratification of the patterns revealed differences (p<.001) for the PABT pattern (at 3 and 12 months post-PKP seen more often in the ICS group), the mixed pattern (more often seen with the SCAS technique), and for the LS pattern at 12 months which was more commonly seen among ICS eyes.

4.4.12. Change in astigmatism over time for the two treatment groups

Table 4.7 shows astigmatic values with all three measurements (CAVK, keratometry, refraction) at different time intervals for the two groups.

a) Topographic astigmatism (simk) :

Topographic astigmatism decreased significantly (F=8.01, p=0.000) across the four measurements at different post-PKP intervals, irrespective of suturing group [Figure 4.9]. Selective sutures removal has resulted in a continuous decrease of the mean topographic astigmatism (simk) for the ICS group from the third to the 12th month post-PKP [Table 4.7]. In the SCAS group, the early topographic astigmatism before suture adjustment started, was 7.21 ± 3.70 D (range 1.2 to 16.7 D). This was significantly reduced (p=0.0007) by the third post-PKP month to 4.56 ± 3.46 D, as suture adjustment in this group starts earlier than the third postoperative month. There was no main effect of suturing technique (F=0.63, p=0.431) in the topographic astigmatism reduction, and at no time interval there was significant difference in astigmatism between the two groups (p=0.198 at the 12-month interval). A significance in treatment/time interaction was found[1] (F=4.79, p=0.005). At a year after PKP, 66% (31/47) of the eyes in the ICS group and 58% (22/38) of the eyes in the SCAS group (p=0.295) were within the astigmatic target of the study (less than 3.5 D).

b) Keratometric astigmatism :

Similar to topographic astigmatism, results were observed for the keratometric astigmatic change [Table 4.7, Figure 4.10]. There was a progressive decrease of astigmatism in the ICS group throughout the first 12 months of the study as sutures were cut. Average keratometric astigmatism was significantly greater for the SCAS group at the pre-adjustment time interval (<3 months) compared to the asigmatism at 3 months (p=0.001). Thereafter, no further reduction was observed (p=0.951, 3 to 12 months post-PKP). However, no significant differences among

[1] this indicates simply that the way that astigmatism changed over time was different for the two groups SCAS and ICS

ICS and SCAS groups were seen (F=0.71, p=0.404 treatment effect, p=0.099 for the 12 month keratometric astigmatism). Treatment/time interaction again was significant (F=7.74, p=0.000). At one year post-PKP, less than 3.5 D of keratometric astigmatism was seen in 65% of the eyes in the ICS group and 56% of the eyes in the SCAS group (p=0.303).

c) Refractive astigmatism :

Time effect on refractive astigmatism (irrespective of treatment group) showed a significant reduction (F=9.59, p=0.000). Treatment effect was not significant (F=0.00, p=0.945), but treatment/time interaction was (F=5.98, p=0.003) [Table 4.7, Figure 4.11], as with topographic and keratometric astigmatism.

d) Surface Asymetry Index (SAI)

It was found that for the SAI, the change observed during the study reduction from baseline value [Table 4.7] was not significant (time effect F=2.22, p=0.101). A treatment group effect was found however (F=6.19, p=0.015), with the SCAS showing lower SAI values than the ICS group (p=0.03 at 12 months; Figure 4.12). In contrast, the SAI treatment/time interaction was not significant (F=1.77, p=0.165).

e) Surface Regularity Index (SRI)

The reduction of SRI over post-PKP time was significant (F=10.19, p=0.000). No main effect of treatment group was seen (F=3.21, p=0.077), although there is a significant difference (p=0.03) for SRI at 12 months between ICS and SCAS groups. Treatment/time interaction was not significant (F=0.46,p=0.693, Fig.4.13).

4.4.13. Effect of timing of suture manipulation on astigmatism

Change in net astigmatism was also analysed as a function of time after PKP [Figure 4.14, Table 4.8]. There was a net change of -2.20 ± 3.29 D in astigmatism for interrupted sutures removed during the first 6 months after PKP, and -0.97 ± 2.66 D for sutures removed during the second 6 months following PKP (p=0.122, NS). For the SCAS group, a significant difference in astigmatism change was found between the first 6 months and the second 6 months post-PKP (-3.10 ± 4.31

vs. -0.45 ± 3.14, p=0.05). No significant differences were found between ICS and SCAS groups for the two time intrervals.

4.4.14. Correlation between initial and final astigmatism

For the ICS group, the correlation of topographic astigmatism at 3 months (before the beginning of suture manipulation) with that of 12 months post-PKP was poor (Spearman correlation coefficient r=0.1804, p=0.225). Similarly, for the SCAS group the correlation between pre-adjustment astigmatism and astigmatism at 12 months was poor (r=0.1401, p=0.402). Large amounts of astigmatism were just as likely as small amounts to be reduced to acceptable levels. Linear regression analysis with best fit lines for the two groups is shown in Figure 4.15.

4.4.15. Stabilization of refraction following penetrating keratoplasty and refractive outcome at 12 months post-PKP

A significantly greater proportion of eyes operated with the SCAS technique reached astigmatic "stability" within the first 3 months following PKP, however from the 6th postoperative month and thereafter, the differences between ICS and SCAS groups were not significant [Table 4.9, Figure 4.16]. The refractive outcome (cylinder D) at 12 months for both groups was very similar. The frequencies of high or low cylinders in the ICS and SCAS groups were not statistically significant (all p values > 0.301 with Fisher's or chi-square, Table 4.10). Figure 4.17 provides information on the frequency of distribution of refractive cylinder one year after PKP in the two groups. The astigmatic goal of less than 3.5 DC was achieved in 73% of eyes in the ICS group and 70% of the eyes in the SCAS group. The incidence of astigmatism above 5 DC, was 10.4% for the ICS group and 15% for the SCAS group.

4.4.16. Other factors affecting astigmatism

Single factor ANOVA was used to compare mean change in astigmatism at 12 months from baseline, among different categories of factors to determine whether any demographic or clinical factors were associated with the amount of astigmatic change. These factors included : Keratoconic vs. non-keratoconic eyes, sex, age ("dichotomised" to the mean age), reoperations vs. first PKPs, surgeon code. No significant effect of any of these parameters was identified.

4.4.17. Complications related to graft suturing

Suture related postoperative complications (other than astigmatism) for the two groups are shown in Table 4.11. In the SCAS group, 18 of the 44 patients (40.9%) had their 10/0 running suture removed because of excessive loosening and suture exposure [Figure 4.18]. In contrast, only 4 of the 51 (7.8%) patients of the ICS group presented with the same complication ($p<.001$). One patient in the ICS group had a spontaneous continuous suture breakage at 5 months post-PKP, but in the SCAS group there was no spontaneous or iatrogenic suture breakage during adjustment[2]. Suture abscesses were infrequent, but two of the SCAS patients developed such a complication, as compared to none of the ICS group ($p=0.211$, NS). Two SCAS patients had to be re-grafted, one as a consequence of epithelial downgrowth (*Karabatsas et al*, 1996b), and the second because the loosening of the 10/0 nylon suture resulted in corneal abscess and subsequent failure of the graft. There were no significant differences among groups for other complications, apart from cheesewiring which was seen only with the SCAS technique ($p<.001$). The overall risk for suture related complications was also found to be significantly higher with the SCAS group than with the ICS groups. Analysis of the results according to preoperative diagnosis (KC vs. non-KC), showed that the combined or independent risk for loose continuous or interrupted sutures, was significantly more ($p<.001$) for the KC than the non-KC patients irrespective of the suturing technique used [Table 4.12]. Additionally, a significantly greater proportion of KC patients developed a loose exposed running suture when operated upon with the SCAS than with the ICS technique. In the SCAS group 65% (13/20) of the KC patients demonstrated an exposed continuous suture, as compared to 21% (4/19) of the KC eyes in the ICS group ($p<.001$).

[2]infact one patient of the SCAS group during the pilot study (not included), experienced iatrogenic breakage during suture adjustment at 9 months post-PKP and required eventually regrafting because of resulting excessive astigmatism (>15 D) due to wound dehiscence.

Postoperative suture adjustment was also found to be associated with loosening of the nylon suture ($p<.001$); of the 32 patients in the SCAS group that had one or more suture adjustments during the follow up, 18 (56.2%) developed loosening of the 10/0 nylon suture, as compared to only 1/12 (8.3%) eyes in the SCAS group that did not require any suture adjustment ($p<.001$).

4.4.18. Effect of continuous nylon suture removal on astigmatism

Single continuous 10/0 nylon suture had to be removed because of loops exposure in a total of 19 cases operated with the SCAS technique, within the 12 months follow up period. In two more cases the 10/0 continuous nylon suture was removed for other reasons[3]. Additionally, there were also 5 cases in the ICS group that required removal of the 11/0 continuous nylon suture within the 12 months following PKP. The average time of suture removal in the SCAS group was 7.6 months post-PKP (SD:3.3 months, range 3.5-12 months). Within the SCAS group, there was no difference in the time of suture removal between previously adjusted and non-adjusted eyes. The median time for removal in the adjusted group was 31 weeks (range 19 to 52 weeks), and for the non-adjusted SCAS sub- group also 31 weeks (range 21 to 50 weeks). For the ICS group the mean time of suture removal was 7.4 months (SD:5.4 months, range 2.5-12 months). The effect of the continuous suture removal for both groups of patients is shown in Table 4.13. No significant differences between the two groups were seen for net or vector astigmatic change, or change in angle of steep meridian.

4.4.19. Examples

Figures 4.19 to 4.21 illustrate three examples of topographic pattern changes seen in patients of the two treatment groups.

4.4.20. Case report

A 78-year-old female patient who had a third PKP for aphakic bullous keratopathy and iris fixation of an IOL using the SCAS technique, developed a

[3]in one case the suture was removed in order to create a more regular cornea and fit a contact lens, and in the second the suture was removed in order to stop a chronic aqueous leak.

suture track leak postoperatively. Attempts to ease the tension on the suture track reduced the astigmatism and stopped the leak albeit only temporarily. Eight months after the procedure, epithelial downgrowth was noted on the corneal graft on both sides of the leak site and intraocular pressure was elevated. A fourth PKP combined with a trabeculectomy was performed. In this case, although a suture track leak was noted following PKP and was therefore a risk factor, suture adjustment may have introduced epithelial cells into the anterior chamber (*Karabatsas et al,* 1996b).

TABLE 4.1 : Surgical procedures performed

	ICS (n=51) No. (%)	SCAS (n=44) No. (%)
PKP alone	30 (58.8%)	28 (63.6%)
PKP and:		
Cataract extraction with IOL implantation	17 (33.3%)	11 (25%)
Cataract extraction, IOL, pupilloplasty	1 (1.9%)	1 (2.3%)
Cataract extraction, anterior vitrectomy (No IOL)	1 (1.9%)	-
IOL exchange, anterior vitrectomy, sulcus supported IOL	-	1 (2.3%)
IOL exchange, anterior vitrectomy, iris sutured IOL	1 (1.9%)	2 (4.5%)
IOL exchange, anterior vitrectomy, synechiolysis, iris sutured IOL	-	1 (2.3%)
AC IOL removal, anterior vitrectomy	1 (1.9%)	-

TABLE 4.2 : Demographic characteristics of patients

	ICS (n=51) No. (%)	SCAS (n=44) No. (%)
Age (yr)		
< 20	2 (4.5%)	2 (3.9%)
20-44	16 (36.4%)	17 (33.3%)
45-64	7 (15.9%)	9 (17.6%)
≥ 65	26 (59%)	16 (31.4%)
mean (range)	57.1 (18-89)	50.5 (18-85)
Sex		
Male	18 (35.3%)	21 (47.7%)
Female	33 (64.7%)	23 (52.3%)
Eye		
Right	22 (43.1%)	14 (31.8%)
Left	29 (56.9%)	30 (68.2%)

ICS : Interrupted + Continuous surgical technique
SCAS : Single continuous adjustable suture

TABLE 4.3 : Preoperative diagnosis of recipient corneal disease

Diagnosis	ICS No. (%)	SCAS No. (%)
Keratoconus	18 (35.3%)	20 (45.4%)
Fuchs' endothelial dystrophy	10 (19.6%)	4 (9%)
Corneal decompensation	5 (9.8%)	3 (6.8%)
Pseudophakic Bullous Keratopathy (PBK)	3 (5.9%)	3 (6.8%)
Aphakic Bullous Keratopathy (ABK)	-	1 (2.2%)
Failed graft	6 (11.7%)	4 (9%)
Herpes Simplex Keratitis (HSK)	3 (5.9%)	3 (6.8%)
Interstitial keratitis	2 (3.9%)	2 (4.5%)
Posterior keratoconus	1 (1.9%)	-
Repeat PKP for high astigmatism	1 (1.9%)	-
Corneal scarring (leukoma)	1 (1.9%)	1 (2.2%)
Reiss-Buckler dystrophy	1 (1.9%)	-
Corneal melt	-	1 (2.2%)
Acanthamoeba keratitis	-	2 (4.5%)
Total	51	44

ICS : Interrupted + Continuous surgical technique
SCAS : Single continuous adjustable suture

TABLE 4.4 : Effect of suture manipulation on topographic astigmatism (simk)

No. of interrupted ROS	No. of eyes	astigmatism (D) immediately before ROS or suture adjustment (d ± SD)	astigmatism (D) after ROS or suture adjustment (d ± SD)	net change in astigmatism (D) (d ± SD)	range of net change (D)	90% net change interval (D)	vectorial change (D) d ± SD (range)
One	15	5.9 ± 3.07	3.76 ± 2.83	-2.14 ± 1.83	-5.3 to 1.8	-2.97 to -1.31	3.81 ± 3 (0.1-10.3)
Two(in same meridian)	13	4.52 ± 1.79	4.8 ± 1.67	+0.28 ± 1.80	-2.7 to 3.7	-0.61 to 1.17	5.46 ± 3.1 (0.8-10.7)
Two (in any meridian)	16	6.6 ± 2.6	5.03 ± 3.14	-1.56 ± 3.75	-7.5 to 4.8	-3.21 to 0.08	6.46 ± 3.1 (2.3-13.2)
Three	19	7.74 ± 3.77	4.6 ± 3.15	-3.14 ± 3.69	-12.5 to 3.8	-6.44 to 0.72	7.36 ± 5.5 (1.2-18.9)
Four	5	8.68 ± 1.03	5.82 ± 4.63	-2.86 ± 3.76	-5.6 to 3.3	-4.61 to 1.67	7.96 ± 3 (5.5-12.8)
Five	6	8.48 ± 3.19	6.01 ± 3.79	-2.46 ± 3.19	-6.8 to 1.7	-5.00 to 0.15	9.58 ± 3.9 (2.3-13.6)
Six	1	8.00	5.50	-2.50			
Total with ICS	**75***	**6.69 ± 3.11**	**4.76 ± 2.99**	**-1.92 ± 3.18**	**-12.5 to 4.8**	**-2.53 to -1.3**	**6.28±4.14 (0.1-19)**
Total with SCAS	**55***	**7.18 ± 3.12**	**4.46 ± 3.24**	**-2.71 ± 4.24**	**-6.90 to 12.8**	**-3.66 to -1.76**	**7.40±4.17 (1.2-18)**

* There are more than 51/44 eyes listed, since some eyes had several sutures removed / or sutures adjustments during the study period.
ROS: removal of sutures; ICS: interrupted+continuous suturing; SCAS: single continuous adjustable suture

TABLE 4.5 : Direction of change in topographic astigmatism (simk) after removal of sutures or suture adjustment in single visits.

Change in astigmatism (D)	No. of visits ICS	SCAS	Fisher's exact test
change < 1 D	14 (18.7%)	5 (9%)	p=0.16
increase 1 to 2.90 D	7 (9.3%)	2 (3.6%)	p=0.18
increase ≥ 3 D	6 (8%)	7 (12.8%)	p=0.27
decrease 1 to 2.90 D	24 (32%)	15 (27.3%)	p=0.52
decrease ≥ 3 D	24 (32%)	26 (47.3%)	p=0.05*
Total	75 (100%)	55 (100%)	

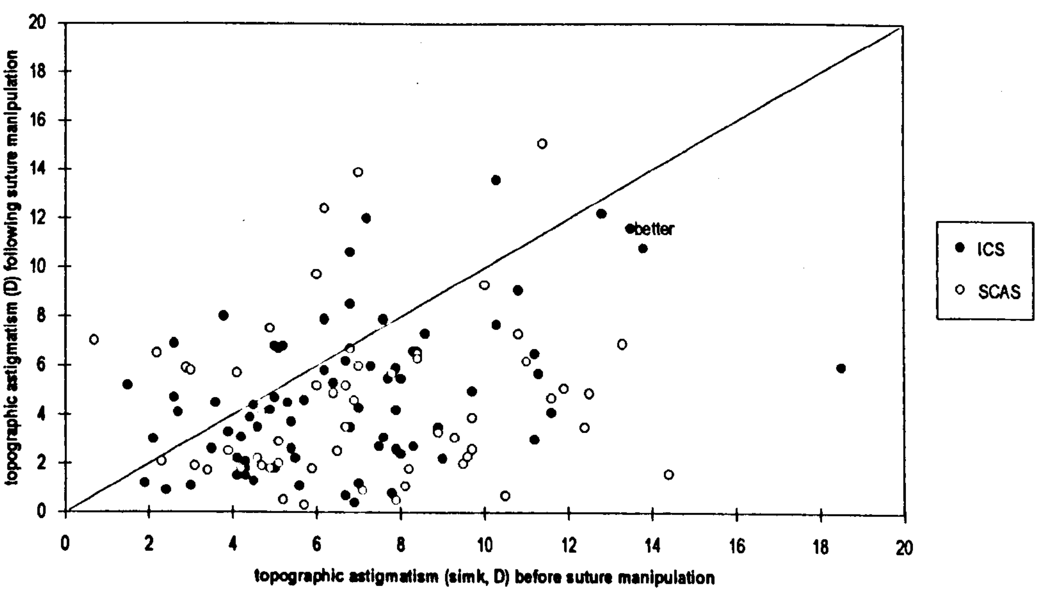

Figure 4.7 : Change in astigmatism by suture manipulation

TABLE 4.6 : Incidence of topographic patterns at different time intervals

	patterns in ICS group		patterns in SCAS group		
time post-PKP	Regular No. (%)	Irregular No. (%)	Regular No. (%)	Irregular No. (%)	*p* value
3 months	23/48 (48%)	25/48 (52%)	13/44 (29.5%)	31/44 (70.5%)	<.001
6 months	19/50 (38%)	31/50 (62%)	15/42 (35.7%)	27/42 (64.3%)	0.496
9 months	17/46 (37%)	28/46 (61%)	12/38 (31.6%)	23/38 (60.5%)	0.466
12 months	11/47 (23.4%)	35/47 (74.5%)	9/38 (23.7%)	26/38 (68.4%)	0.526

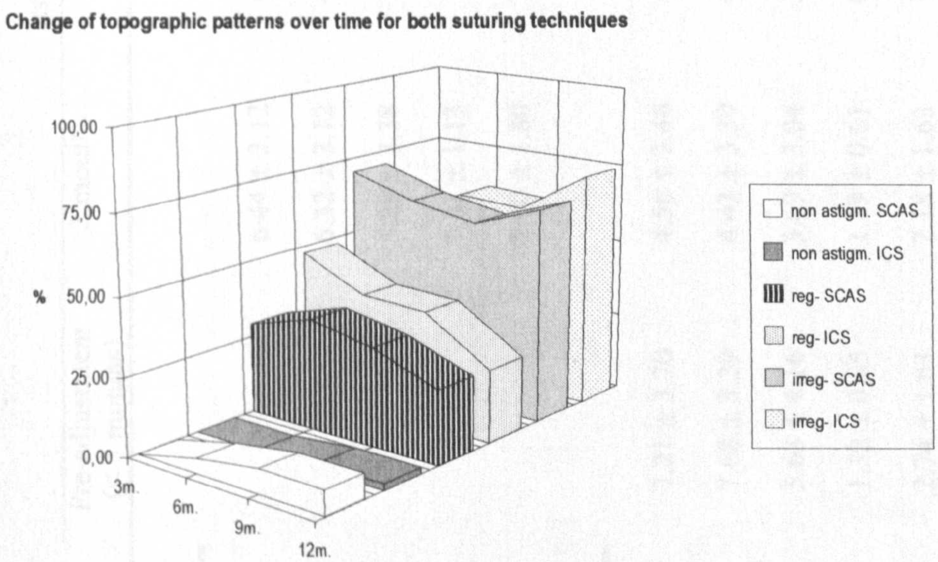

Figure 4.8 : Change of post-PKP topographic patterns over time, for both suturing techniques.

TABLE 4.7 : Astigmatism at various times following PKP, in the two suturing groups.

	astigmatism (D) (mean ± SD)				
	Pre-adjustment (< 3 months)	3 months	6 months	9 months	12 months
ICS group					
Simk (D)		6.44 ± 3.12	4.65 ± 3.31	3.95 ± 2.08	3.39 ± 1.91
Keratometry (D)		6.32 ± 3.12	4.26 ± 2.94	3.78 ± 1.82	3.26 ± 1.81
Refractive cylinder (D)		5.29 ± 3.38	2.94 ± 1.96	2.67 ± 2.02	2.66 ± 1.70
SAI		1.61 ± 1.13	1.48 ± 0.87	1.22 ± 0.72	1.26 ± 0.68
SRI		2.60 ± 1.80	2.54 ± 1.93	1.95 ± 1.63	1.66 ± 1.31
SCAS group					
Simk (D)	7.21 ± 3.70	4.56 ± 3.46	4.29 ± 3.01	4.37 ± 3.23	4.14 ± 3.10
Keratometry (D)	7.68 ± 3.29	4.43 ± 3.39	4.33 ± 3.50	4.44 ± 3.53	4.49 ± 3.34
Refractive cylinder (D)	5.63 ± 4.16	3.69 ± 3.04	3.36 ± 2.06	3.85 ± 3.09	3.12 ± 2.62
SAI	1.32 ± 0.65	1.19 ± 0.61	0.99 ± 0.52	1.21 ± 0.83	0.93 ± 0.53
SRI	2.74 ± 1.63	2.18 ± 1.63	1.64 ± 1.31	1.65 ± 1.35	1.17 ± 0.66

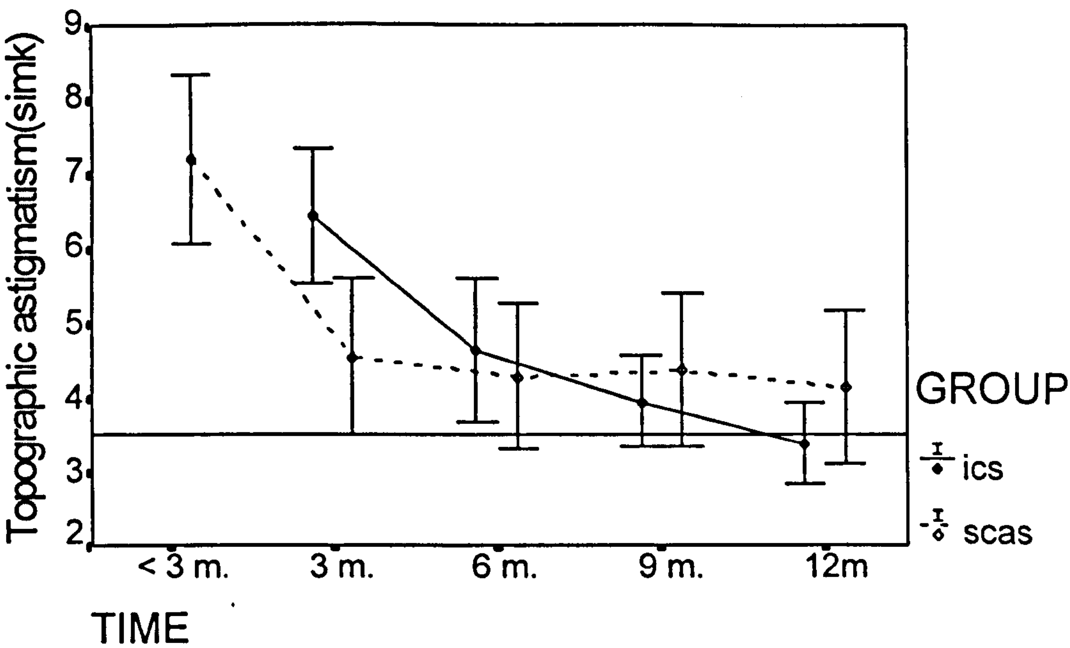

Figure 4.9 : Postoperative evolution of mean topographic astigmatism (simk, D) for the two treatment groups. Error bars denote 95% confidence intervals. The horizontal line indicates the target of 3.5 D postoperative astigmatism.

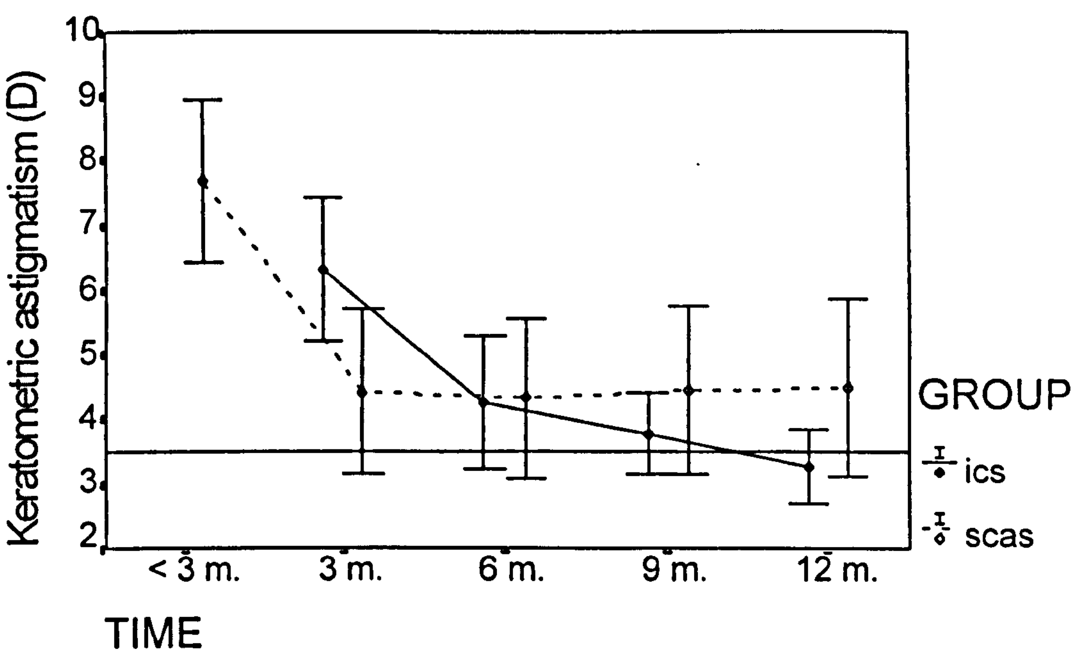

Figure 4.10 : Change of mean keratometric astigmatism (D) with time, for the two groups. Error bars denote 95% confidence intervals. The horizontal line indicates the target of 3.5 D postoperative astigmatism.

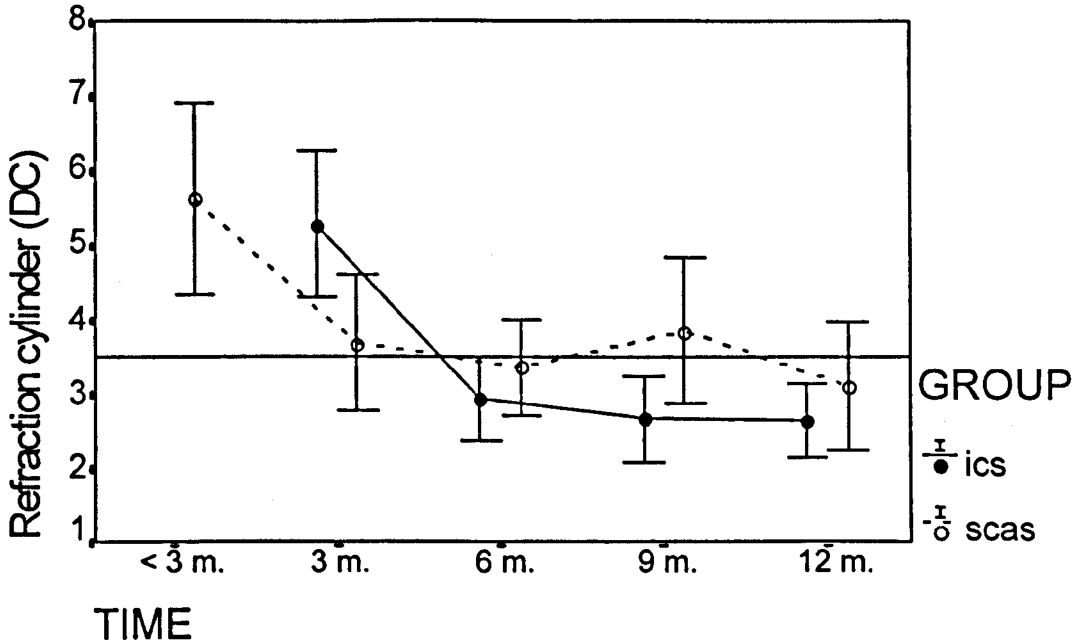

Figure 4.11 : Postoperative evolution of mean refractive astigmatism (cyl D) over time. Error bars denote 95% confidence intervals. The horizontal line indicates the target of 3.5 D postoperative astigmatism.

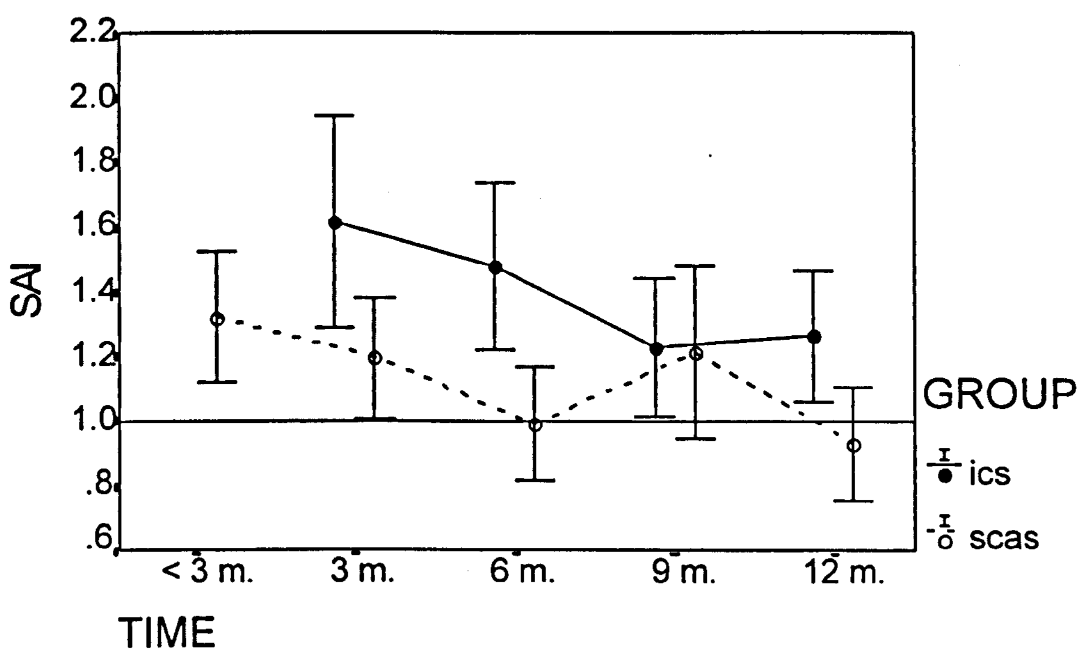

Figure 4.12 : Effect of suture manipulation on SAI, for the two groups over the postoperative time.

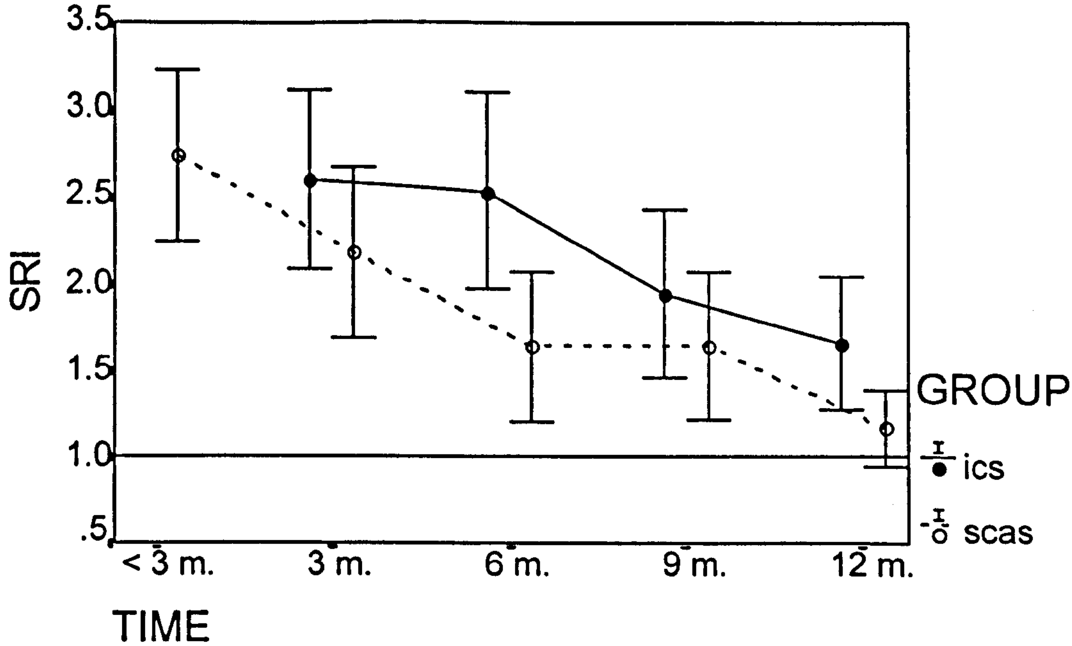

Figure 4.13 : Postoperative evolution of SRI

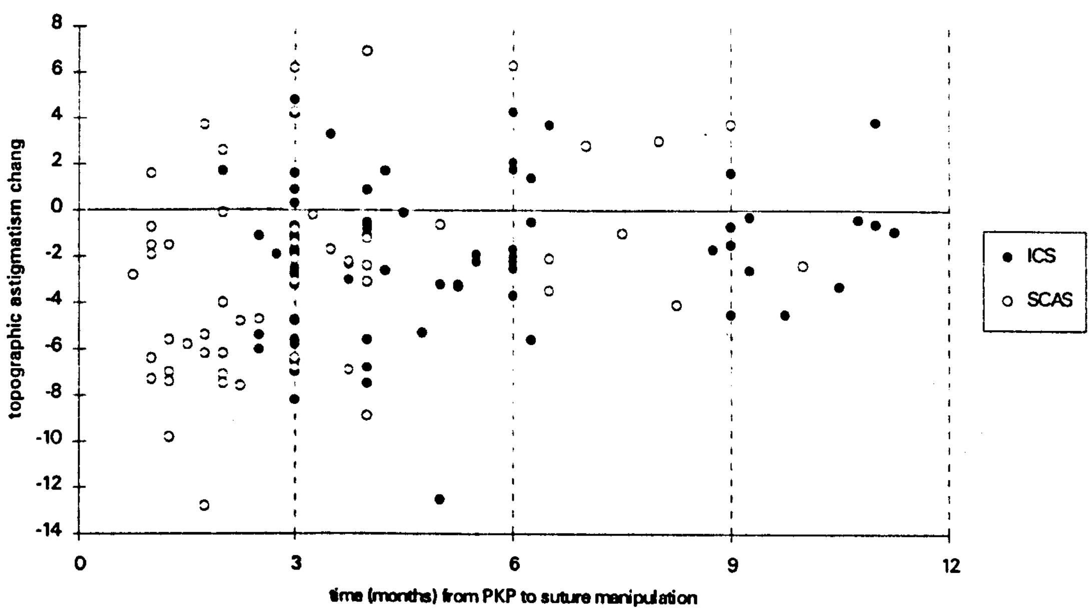

Figure 4.14 : Change of post-PKP topographic astigmatism in relation to time of suture manipulation.

TABLE 4.8 : Effect of timing of suture manipulation on post-PKP astigmatism.

	Time post-PKP (months) of suture manipulation	No. eyes	net change (D) (mean ± SD)	*p* value
ICS	0-6 m.	58	-2.20 ± 3.29	0.122
	6-12 m.	17	-0.97 ± 2.66	
SCAS	0-6 m.	47	-3.10 ± 4.31*	0.05
	6-12 m.	8	-0.45 ± 3.14*	

* indicates statistically significant difference

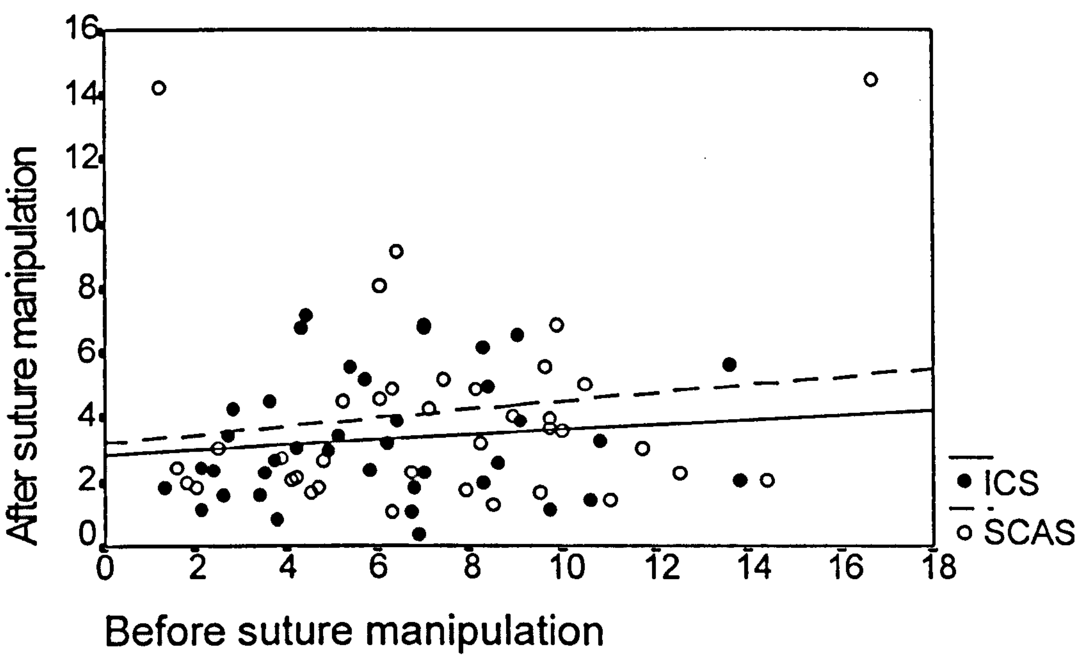

Figure 4.15 : Correlation for initial astigmatism (before suture manipulation), and final astigmatism (after completion of suture adjustments for SCAS, or removal of interrupted sutures for ICS). Regression lines for the two groups are also shown.

TABLE 4.9 : Time to refractive stability

months post-PKP	ICS (n=47) No. (%)	SCAS (n=38) No. (%)	*p* value (Fisher's)
< 3 months	2 (4.2%)	8 (21%)	0.019
< 6 months	21 (44.7%)	21 (55.3%)	0.226
< 9 months	30 (63.8%)	25 (65.8%)	0.517
< 12 months	38 (80.8%)	35 (92.1%)	0.120

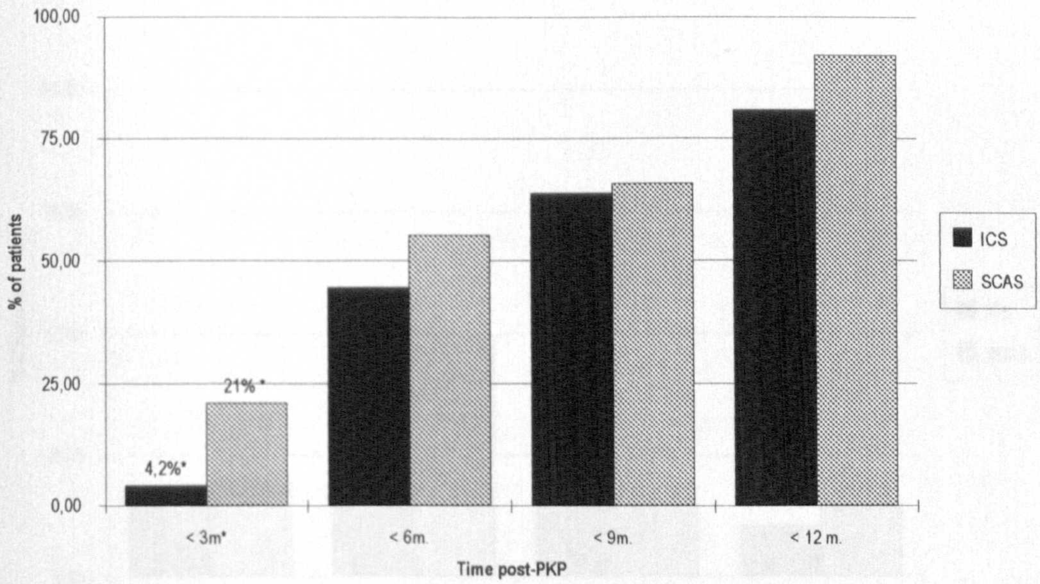

Figure 4.16 : Stabilisation of refraction following PKP
(* indicates statistical significance)

TABLE 4.10 : Refractive outcome at 12 months postPKP

Refractive cyl.(D)	ICS No. eyes (%)	SCAS No. eyes (%)	*p* value
< 0.50 D	1 (2%)	2 (5%)	NS
0.50 - 1.00 D	7 (14.6%)	6 (15%)	NS
1.25 - 2.00 D	13 (27%)	8 (20%)	NS
2.25 - 3.50 D	14 (29.2%)	12 (30%)	NS
3.75 - 5.00 D	8 (16.6%)	6 (15%)	NS
> 5.00 D	5 (10.4%)	6 (15%)	NS
Total	48	40	

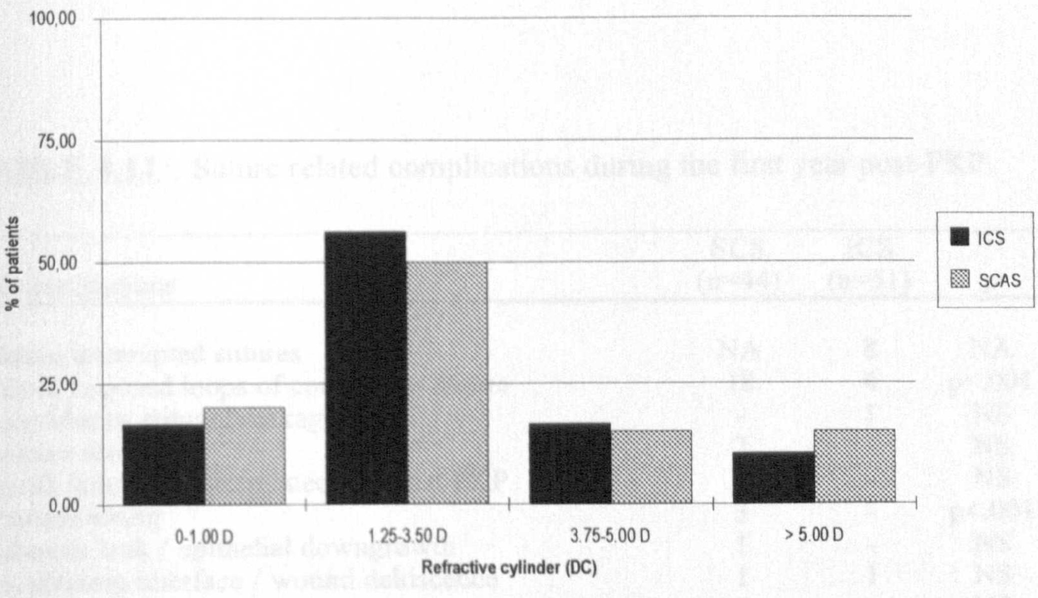

Figure 4.17 : Distribution of refractive cylinder at 12 months following PKP.

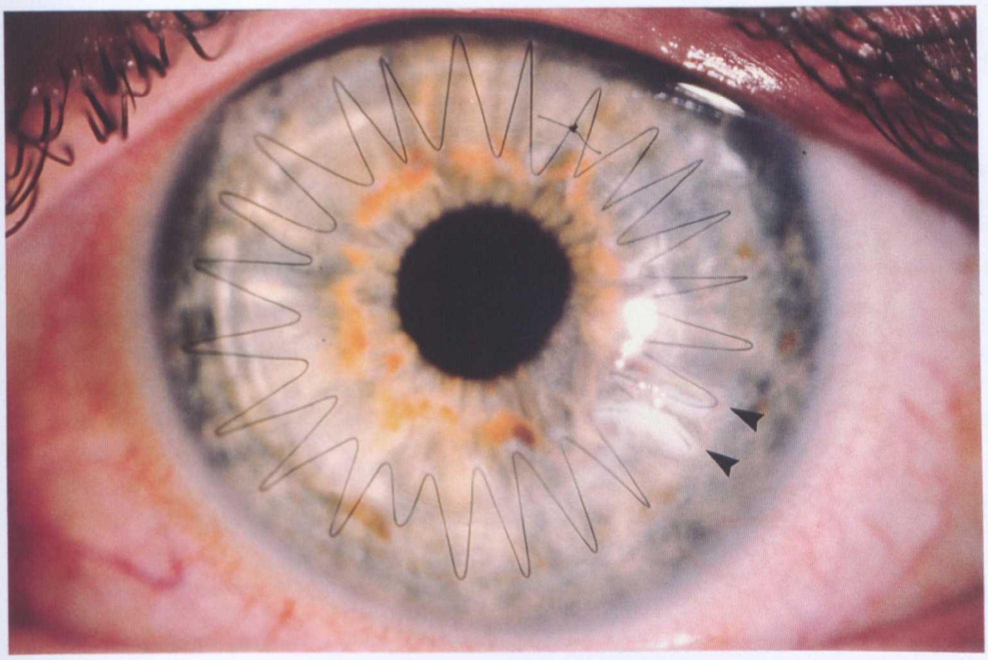

Figure 4.18 : Photo of an eye operated with the SCAS technique, showing two loose exposed loops of the single running 10/0 nylon suture, at 5 months following penetrating keratopalsty.

TABLE 4.11 : Suture related complications during the first year post-PKP.

Complications	SCS (n=44)	ICS (n=51)	*p*
loose interrupted sutures	NA	8	NA
loose exposed loops of continuous suture	18	4	p<.001
continuous suture breakage	-	1	NS
suture abscess	2	-	NS
graft failure (suture related) / repeat PKP	2	-	NS
cheesewiring	3	-	p<.001
chronic leak / epithelial downgrowth	1	-	NS
overriding interface / wound dehiscence	1	1	NS
significant neovascularization	2	-	NS
total no. of eyes with suture related complications*	26	14	p<.001

** total no. less than the arithmetic sum of 29, because 3 eyes had a combination of complications*

NA: not applicable, NS: not significant

TABLE 4.12 : Suture related complications during the first year post-PKP, according to preoperative diagnosis

Complications	KC (n=39)	non-KC (n=56)	*p*
Loose interrupted sutures only	7	1	p<.001
loose continuous suture only	17	5	p<.001
spontaneous continuous suture breakage	1	-	NS
loose continuous /or interrupted sutures (combined risk)	24	6	p<.001
suture abscess	-	2	NS
cheesewiring	1	2	NS
total no. of eyes with suture related complications	26	10	p<.001

KC : keratoconus, non-KC : non keratoconus

TABLE 4.13 : Effect of 10/0 or 11/0 nylon suture removal on astigmatism

	No. eyes	net change (D) (mean ± SD) (range)	angle change (°) (mean ± SD) (range)	vector change (mean ± SD) (range)
SCAS 10/0 nylon	15	1.35 ± 5.69 (-8.2 to 15.5)	21 ± 17.6 (3-59)	5.27 ± 4.35 (0.8-17.2)
ICS 11/0 nylon	5	-0.85 ± 2.21 (-4 to 0.7)	15 ± 15.5 (5-38)	2.78 ± 1.70 (1.3 to 4.4)
p value		0.252	0.542	0.100

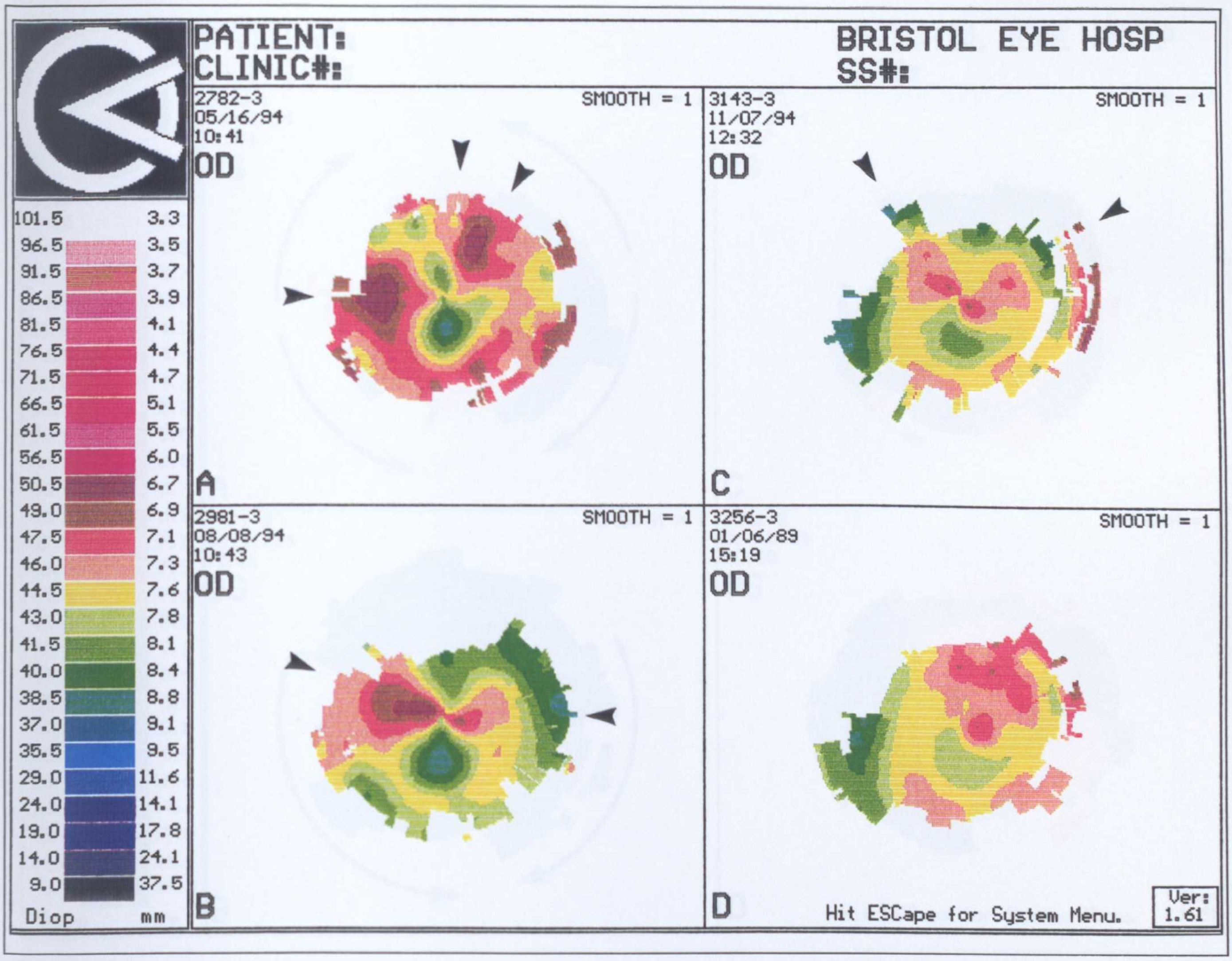

Figure 4.19 : An example of the 'suture removal roulette' involved in the management of postkeratoplasty astigmatism with the ICS technique. Sequential removal of selective interrupted sutures (position indicated by the arrows) reduced significantly the postoperative astigmatism.
At 12 weeks post-PKP, topographic astigmatism measured 4.00 D. By selective removal of three interrupted sutures at 9, 12 and 1 clock positions (figure A), astigmatism increased to 7.8 D at 24 weeks (figure B). Further selective suture removal at that time and at 36 weeks post-PKP (figure C), reduced corneal astigmatism to 0.9 D at 12 months following the keratoplasty (figure D).

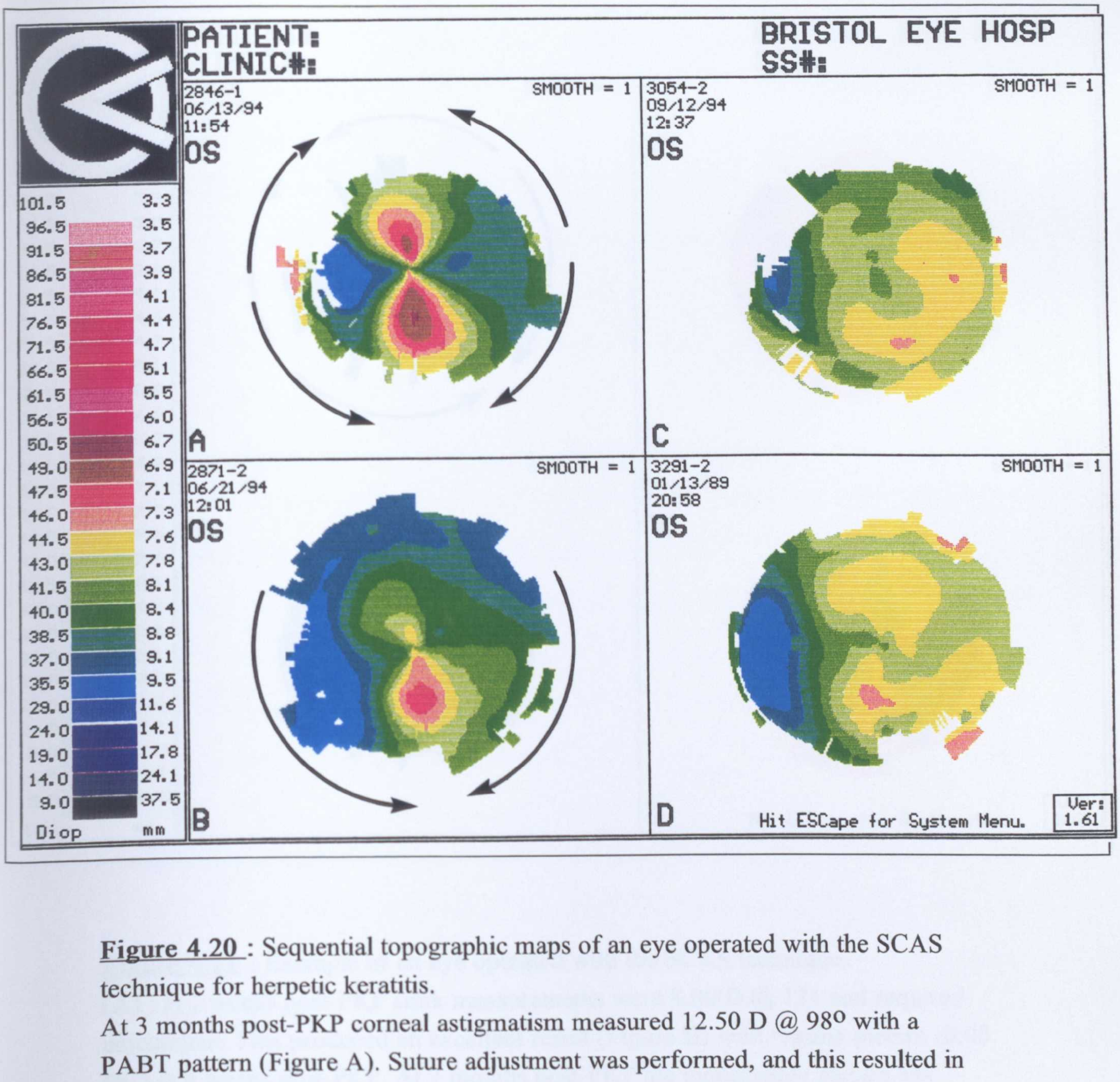

Figure 4.20 : Sequential topographic maps of an eye operated with the SCAS technique for herpetic keratitis.

At 3 months post-PKP corneal astigmatism measured 12.50 D @ 98° with a PABT pattern (Figure A). Suture adjustment was performed, and this resulted in reduction of astigmatism to 4.7 D @ 97° (Figure B). Re-adjustment was performed at 3.5 months post-PKP that produced a regular non astigmatic topographic pattern (1.00 D @ 38°) at 6 months post-PKP (Figure C). Topographic examination at 12 months post-PKP (Figure D) shows a steep/flat (SF) pattern with 2.00 D @ 79° corneal astigmatism.

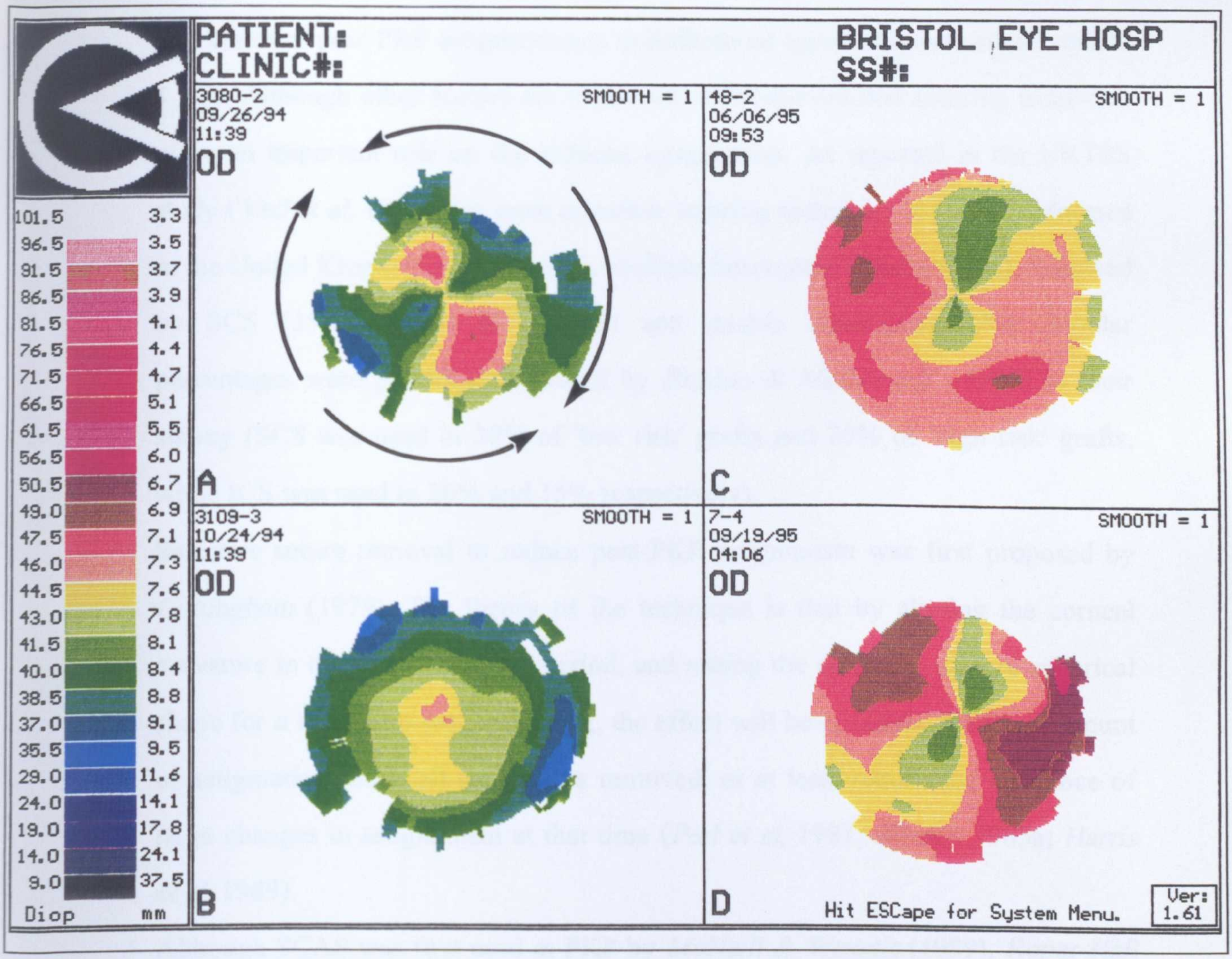

__Figure 4.21__ : Example of an eye operated with the SCAS technique.
(A) : at 2 weeks post-PKP simk measurements were 8.00 D @ 121 and required adjustment. This produced an excellent result (Figure B) with regular picture (0.00 DC) at 4 weeks post-PKP. At 7 months post-PKP the topographic picture has changed dramatically (Figure C), as a result of loosening of the single continuous suture that has produced an astigmatism measuring 4.20 D @ 167. The excessively loose suture had to be removed. At 12 months post-PKP (Figure D), astigmatism was back to 6.80 D @ 150, with the steep semimeridians at about the same axis as in Figure A.

The case indicates the "corneal tissue memory". The initial astigmatism (figure A) is likely to be due to tissue compression at axis 121. This could be evened out by suture adjustment, but following suture removal, areas of tissue compression (or tissue strech) which have healed might lead to reoccurence of the original astigmatism which had only been masked or temporarised by suture adjustment.

4.5. Discussion

The cause of post-PKP astigmatism is multifactorial (general introduction, section 1.5.3). Although other factors are important, it is believed that suturing technique plays an important role on the induced astigmatism. As reported in the UKTSS study (*Vail et al,* 1996), the most common suturing technique in PKPs performed in the United Kingdom and Ireland is multiple interrupted sutures (42%), followed by SCS (35%), mixed ICS (17%) and double continuous (6%). Similar percentages were previously reported by *Burdon & McDonnell* (1995) in their survey (SCS was used in 39% of 'low risk' grafts and 25% of 'high risk' grafts, while ICS was used in 20% and 15% respectively).

Selective suture removal to reduce post-PKP astigmatism was first proposed by *Cottingham* (1979). The theory of the technique is that by altering the corneal curvature in the early post-PKP period, and setting the cornea in a more spherical shape for a long-term wound healing, the effect will be to reduce the final amount of astigmatism when all sutures are removed, or at least reduce the incidence of large changes in astigmatism at that time (*Perl et al,* 1981; *Binder,* 1985a; *Harris et al,* 1989).

Although SCAS was first used in PKP by *McNeill & Wessels* (1989), *Roper-Hall* in 1982 had already reported on the use of a continuous suture with easing of tension towards the plus axis, stating in his original paper that the technique can be applied to cataract extraction wounds; after trauma; as well as in keratoplasty, but without presenting any results. He later published (*Atkins & Roper-Hall,* 1985) results from 36 eyes with excessive astigmatism (more than 3.00 D) following cataract extraction, who underwent continuous suture adjustment 6 to 8 weeks postoperatively. Reduction of the astigmatism was seen in 92% of the cases.

Previous independent studies [Table 4.14], have shown that selective removal of interrupted sutures reduces astigmatism; similar results have also been achieved in independent studies with the SCAS technique [Table 4.15]. To-date only one retrospective study (*van Meter et al,* 1991) and one prospective randomised study

TABLE 4.14 : Previous studies with ICS and longitudinal measurements of astigmatism

Study	No. eyes	R/P	astigmatism (D) 3 months	6 months	12 month	variable FU	Follow up (months)	Multiple surgeons	ROS according to	Comments
Perl et al, 1981	61 SS 119OS	R	-	-	-	4.17 SS 6.44 OS	24 m SS 13 m OS	No	Keratometry Refraction	
Stainer et al, 1982	50	R	5.2 ± 3.4	4.3 ± 3.1	5.2 ± 2.8	-	7-19 m	No	Keratometry Corneascope	only 25 eyes with 12m FU
Binder, 1985	204	P	4.1	3.6	3.3	-	8-62 m.	No	Keratometry Corneascope	133 eyes with 12 m FU
Feldman & Brown, 1987	25	R	-	-	-	1.37 ± 0.24 1.52 ± 0.18*	3-21 m	No	Keratometry	selective cases; variable FU
Musch et al, 1989	60	P	4.0	3.0	2.5	-	12 m	Yes	Keratometry	
Pradera et al, 1989	44	R	-	-	-	3.29 ± 1.77	6-30 m (mean 13.5)	No	Refraction Keratometry Photoker'y	PKP+IOL in all cases

Unless otherwise stated, astigmatism is measured with keratometry
* = refractive astigmatism, P=prospective study, R=retrospective study, SS=same size, OS=oversize, FU=follow up, ROS=removal of sutures

TABLE 4.15 : Previous studies with SCAS

Study	No. eyes	R/ P	Astigmatism (D) before adjustment	astigmatism (D) at 3 m's post-PKP	astigmatism (D) at 6 m's post-PKP	astigmatism (D) at variable FU	Follow up	No. of surgeons	suture adjustment according to..	Comments
McNeill & Wessels, 1989	330	R.	5.32 ± 3.13 (< 3m.)	2.87 ± 1.87 (3 - 6 m.)	3.23 ± 1.95 (> 6 m.)	3.58 ± 2.27 (sutures out)	mean 19.3 m.	1	> 3 D Keratometry	No info. on Δ
Lin et al, 1990b	8	P.	6.7 ± 2.3 (simk)	1.9 (simk)	-	1.7 ± 0.7 (simk)	4 m.	4	> 2.5 D CAVK	small FU only 8 eyes KC excluded
Nabors et al, 1991	52	R	9.97 ± 3.31	-	-	1.89 ± 2.23	mean 13 weeks	not specified	> 4.5 D Keratometry	64% <3m. FU No info. on Δ
Temnycky et al, 1991	33	R	8.41 ± 3.50	-	-	2.22 ± 1.96	3-4 m.	1	> 3 D CMS, refr'n Keratometry	small FU 10% of cases excluded
Hope-Ross et al, 1993	39	P	6.33 ± 1.38 (refraction)	-	-	2.69 ± 1.14 (refraction)	not specified	5	> 4 D	no info. on FU only first PKPs
Serdarevic et al, 1994	12* 13§	P	- 4.89 ± 1.99	- -	1.83 ± 0.78 2.72	- -	6 m. 6 m.	1 1	> 3.5 D at 1 m postop	small numbers only 6m FU

Hovding, 1994	19	R	8.20 ± 2.44	-	-	4.75 ± 3.36	not specified	?	> 5 D Keratometry refraction	90% KC eyes only 12 eyes complete data
Chell et al, 1996	30	P	-	-	-	3.25 (0-8) (refraction)	53-170 weeks	5	> 4D	all firts PKPs only refraction

RANDOMISED TRIALS SCAS vs. ICS

Study	No. eyes	R/ P	Preadjustm. or pre-ROS astigmatism	6 months	variable FU	Follow up	No. surgeons	suture adjustment according to	Comments
van Meter et al, 1991	26 SCAS	R	6.5 ± 4.4	-	1.5 ± 1.1	6 - 24 m.	1	> 3 D CMS, keratometry photoker'y	variable FU retrospective study only 12% KC
	31 ICS		8.4 ± 3.8	-	3.2 ± 1.9	15 - 28 m.	1		
Filatov et al, 1993	18 SCAS	P	5.4 ± 3.7	3 ± 2.4	2.7 ± 2.2	~ 9 m.	1	keratometry	short FU
	20 ICS		6.5 ± 4.3	4.2 ± 2.2	3.9 ± 2.5	min 6 m.	1	photokerat'y TMS	all KC patients in ICS
Filatov et al, 1996	16 SCAS	P	-	-	3.1 ± 1.3	28-60 m.	1	"	all KC patients in ICS
	16 ICS		-	-	3.3 ± 1.4 (refraction)	23-59 m.	1	"	refractive astigmatism

Unless otherwise stated, astigmatism is measured with keratometry

* with intraoperative adjustment, § postoperative adjustment, Δ: diagnosis, P: prospective study, R: retrospective study, FU:follow up, KC:keratoconus, ROS: removal of sutures

(*Filatov et al,* 1993 and 1996) have been published comparing astigmatic results of the two techniques. The question as to whether a certain suturing technique results in higher postoperative astigmatism than another, can only be answered by formal prospective controlled randomised clinical trials, which have powerful study designs to eliminate the uncertain effects of bias and confounding (*Evans,* 1995). Although in this study, the participation of 6 surgeons might have introduced some bias, from a practical point of view it is probably more important to know the efficacy of a certain technique in surgical hands of variable skill. In that respect, this represents a strength rather than a weakness of the present study. Besides, analysis of variance showed that the surgical expertise level did not affect the astigmatic outcome. The two suturing groups were comparable preoperatively (Tables 4.1 to 4.3). In particular, factors such as the perioperative use of IOL were evenly distributed between the two groups. The possible contribution of malposition of scleral supported IOL to overall astigmatism (*Hardten et al,* 1993) was avoided by using the technique of iris sutured IOL for the 4 cases that posterior capsula support was not available. For the rest of the triple procedures (30 cases), the IOL was inserted into the bag. Furthermore, in order to minimize the potential effect of a trephine tilt on post-PKP astigmatism (*Krumeich et al,* 1988), a Hessburg-Baron suction trephine was used in every case.

Direct comparison with previous studies presents the difficulties of variable confounds. In the original SCAS technique publication (*McNeill & Wessels,* 1989) 17 to 26 bites were used in various cases; other surgeons have used 16 bites (*Lin et al,* 1990b; *Hope-Ross et al,* 1993), or 20 to 24-bite suture (*van Meter* 1991; *Temnycky et al,* 1991; *Hovding* 1994; *Serdarevic et al,* 1994). In the present study a 24-bite running suture was used in every case, to keep the group as homogeneous as possible. Whether the number of bites plays a role in the suture adjustment or the outcome, is not known. Time of adjustment also varies in the various reports. Successful suture adjustment has been reported from the first postoperative day (*McNeill & Wessels,* 1989) to up to 19 months after PKP

(*Hovding,* 1994). According to *Serdarevic et al.* (1994) the optimum time appears to be intraoperatively. Common practice however among corneal surgeons in the UK, is for continuous sutures to be adjusted on average 2.6 months following PKP (range 2 weeks to 6 months), whereas selected interrupted suture removal takes place on average 3.9 months (range 1-12 months) post-PKP (*Burdon & McDonnell,* 1995). In our series the mean time for suture adjustment was 3.2 months (13 weeks) with range from 3 to 40 weeks post-PKP, whereas interrupted sutures were removed later (mean 20.6 weeks, range 10 to 52 weeks post-PKP). Therefore these differences in the timing of suture manipulation invalidate direct comparison of the two groups on the early postoperative period up to 20 weeks, since one group had already had adjustment whereas the other had not.

There is also no common agreement as to what is the ideal suture adjustment technique. *McNeill & Wessels* (1989), *Lin et al.* (1990b), *Filatov et al.* (1993), and *Serdarevic et al.* (1994), advocated adjustment on the slit lamp without disruption of the wound interface, while *van Meter et al.* (1991) and *Nabors et al.* (1991) opened the wound up to the superficial stroma with the platform of the tying forceps. There are no control randomised trials in the literature to favour one or the other practice. *Serdarevic* (1994) believes that overcorrection with change in axis should be avoided during adjustment because the effect usually increases over a few days. There is no hard evidence to support that, as topographic evaluation immediately after the adjustment is not useful, because of the rough surface resulting from the epithelial break. Although *McNeill & Wessels* (1989) originally suggested leaving the suture slightly loose after adjustment, this should be avoided as very loose loops may delay or even preclude epithelial resurfacing and increase the risk of mucous accumulation and infection. On the other hand, the experience of the present series is in agreement with *Serdarevic* (1994), that adjustment is difficult and often unsuccessful when the running suture is excessively tight or the loops are unevenly spaced.

The minimum amount of astigmatism where suture adjustment is justified, varies among studies. Most authors advocate adjustment when astigmatism is over 3 D (*McNeill & Wessels*, 1989; *Temnycky et al*, 1991; *van Meter et al*, 1991). Others, used lower or higher cutpoints (*Lin et al*, 1990b - at 2.5 D; *Hope-Ross et al*, 1993 - at 4 D; *Hovding*, 1994 - at 5 D). In the present study it was decided to use the 3.5 D as a target for both the ICS or the SCAS techniques, because this is an amount of astigmatism that is tolerated by the patient with glasses, it is also correctable with contact lenses and we would not proceed to surgical correction of astigmatism at this level.

Number of necessary suture manipulations

McNeill & Wessels (1989) reported that 205/330 (62%) of their cases required adjustment, an average of 1.51 adjustments per case. *Serdarevic et al.* (1994) observed that 77% of the patients without intraoperative adjustment required postoperative adjustment to reduce astigmatism below 3.5 D, and this is in accordance with the present study where suture adjustment was required in 78.3% of the eyes (one adjustment in 38%, two adjustments in 26%, three adjustments in 14.3%). In a comparative study, *Filatov et al.* (1993) found that the number of visits differed between the two groups. The SCAS technique required fewer suture manipulations. In 44% of patients with SCAS and 25% with ICS no suture manipulation was necessary. In contrast, a retrospective non-randomised study (*Van Meter et al*, 1991) indicated that SCAS offers the advantage of fewer postoperative suture manipulations and earlier optical stability than ICS (0.9 ± 0.7 adjustments per patient for the SCAS vs. 3.8 ± 1.8 suture manipulations for the ICS). In that study, 26% of the SCAS patients required no suture manipulation, as compared to 6% of the ICS patients. In our prospective study no significant difference was observed between the two groups (1.5 vs. 1.25 visits for suture manipulation per patient for the ICS and SCAS groups respectively). However, our results on incidence of patients not requiring suture manipulation match those of *van Meter et al.* (1991) study.

The role of CAVK on suture manipulation and astigmatism measurement

Post-PKP astigmatism can be radially asymmetric. Therefore, regional differences in corneal topography can be identified better with the colour coded maps than with information obtained from refraction, keratometry, or photokeratoscopy. In particular, the use of CAVK overcomes the limitation of conventional central keratometry, which by intersecting the keratoplasty wound on each side at any given axis, cannot identify which of the two sides of the wound accounts for the astigmatism. The picture obtained with CAVK, helps to define the area for intervention, either by removing the tight sutures, or by adjusting the local tension of the suture [Figures 4.19 to 4.21]. In the case of multiple interrupted sutures, although the steep meridian is usually in alignment with a tight suture that can possibly be identified on slit lamp inspection, this is not always the case. Sutures impose their effects in the form of vectors, so a resultant astigmatic vector is not always at the axis of the tight suture. Tight sutures cause focal tissue compression, indentation of the mires, steepening of the graft and are reproduced as 'hot' colours. The 'suture removal roulette' is greatly facilitated by the use of CAVK [Figure 4.19]. Photokeratoscopy has also been used for this purpose (*Kozarsky & Waring,* 1985; *Burk et al,* 1988; *Binder,* 1988). *Harris et al.* (1989) reported on the ability of keratographs to guide selective removal of sutures when the corneal surface is too rough for accurate keratometric measurements. *Strelow et al.* (1991), found that in 69% (20/29) of cases, the preliminary clinical impression (determined on the basis of keratometry, refraction and inspection of sutures), was changed when the topographic map was considered. Although CAVK has been advocated as useful guide to either selective removal of sutures or adjustment, at present refraction alone or in combination with keratometry is by far the most common method used among UK corneal surgeons to assess post-PKP astigmatism. Only 6% of surgeons use CAVK (*Burdon & McDonnell,* 1995).

In chapter 2 it was shown that keratometry is more reproducible than TMS-1 for highly astigmatic post-PKP corneas. However, as readings rely very much upon surface regularity, in a percentage of cases the mires are very distorted and totally unreliable. For several weeks in the postoperative period, it is difficult to determine keratometric and refractive astigmatism (*Swinger,* 1987). *Filatov et al* (1993) found that early postoperative astigmatism could not be measured in 20% of the patients with ICS because of irregular corneal topography. In another study post-PKP corneal astigmatism was undetermined due to distorted mires in 21% of cases (*Smiddy et al,* 1992). *Khong et al.* (1993) on a study with 8 post-PKP keratoconic corneas observed that the healing corneal graft proved too irregular for consistently interpretable keratometric measurements in the first six months postoperatively. Because of the surface irregularity, keratometry readings were often estimates only. This represents a problem in analysis of all those studies, because corneas with missing data are likely to have high levels of astigmatism. The results are likely to be affected by that, especially in studies with small numbers. The present study suffers with the same weakness of missing keratometric data, but to a much lesser degree. Because of the prospective controlled nature of this study, astigmatism was measured at every visit with refraction and CAVK (no missing data). In addition, the larger number of eyes followed, allows for adequate power in the study.

Previous studies

In accordance with earlier studies [Tables 4.14 and 4.15], the present study confirms that postkeratoplasty astigmatism can be significantly decreased with either adjustment of a single 10/0 nylon suture, or selective removal of interrupted sutures. The magnitude of astigmatic change obtained compares well with those reported earlier. Previously published non-randomised independent series with either the ICS or the SCAS technique (apart from the fact that they cannot offer direct comparison between the two techniques) suffer other weaknesses. Most of these series are retrospective, some of them with small number of eyes studied (*Lin et al,* 1990b; *Serdarevic et al,* 1994; *Hovding,* 1994). A number of studies had too short or unspecified follow up times (*Stainer et al,* 1982; *Feldman &*

Brown, 1987; *Lin et al,* 1990b; *Nabors et al,* 1991; *Temnycky et al,* 1991; *Hope-Ross et al,* 1993; *Hovding,* 1994; *Serdarevic et al,* 1994). In two studies keratoconic patients were excluded from the SCAS group (*Lin et al,* 1990b; *Filatov et al,* 1993) or very few were keratoconic (*van Meter et al,* 1991), whereas in others details on diagnosis were not available (*McNeill & Wessels,* 1989; *Nabors et al,* 1991). Furthermore, in some studies astigmatism was measured only with refraction (*Hope-Ross et al,* 1993; *Chell et al,* 1996). The amount of manifest astigmatism is usually less than that measured with the keratometer (*Troutman & Gaster,* 1980; *Binder,* 1988).

Astigmatism reduction with the two suturing techniques

Direct comparison between ICS and SCAS techniques has only been examined in two previous studies [Table 4.14]. *Van Meter et al.* (1991) reported on a retrospective comparative study of PKPs performed by one surgeon, in which 26 eyes with SCAS were compared to 31 eyes with ICS). The "final" keratometric astigmatism was significantly less for the SCAS group (1.5 ± 1.1 D), compared to the ICS group (3.2 ± 1.9 D), at variable follow ups however between the two groups. These results vary considerably from the ones obtained in the present study, but as the authors point out, there is a danger in drawing conclusions from retrospective studies, especially those with non concurrent controls. In addition, *van Meter et al.* had included very few keratoconic patients (11% in the SCAS, 13% in the ICS), as compared to our population study (36% in the SCAS, 45.4% in the ICS). *Filatov et al,* in 1993 reported the first prospective randomised study of 20 eyes with ICS vs. 18 eyes sutured with SCAS. Although randomisation should have the methodological advantage of balancing the study groups, in that paper all patients with keratoconus (n=5) were allocated to the ICS group. There were also differences among the groups average age, and the variable follow up was as short as 6 months (mean: 8.7 months, min: 6 months). Analysis showed that the SCAS technique resulted in lower 'final' mean postoperative keratometric astigmatism (SCAS: 2.7 ± 2.2 D; ICS: 3.9 ± 2.5 D, P=0.021). The same authors reported on the same patients 2 to 4 years post-PKP, indicating that the early statistically significant differences in astigmatism, did not remain later in the postoperative course (*Filatov et al,* 1996). The authors concluded that the differences observed between their two studies, indicate that the principal benefit of the SCAS lies in its ability to compensate for other sources of astigmatism, but not to influence the shape of the transplant after full healing and suture removal. This is a statement reinforced by this thesis. It has been shown here that the two suturing techniques do not significantly affect the postoperative astigmatism (topographic, keratometric or refractive) during the first year post-PKP. Both techniques reduce significantly the amount of astigmatism, but the way they influence astigmatism (group/time interaction) differs between the two groups. Although at no time interval a significant difference in astigmatism was observed, at 3 months SCAS showed less astigmatism than ICS; the two groups were very similar at 6 months, but at 12 months post-PKP the ICS showed less astigmatism than the SCAS group. There was a continuous decrease of astigmatism with time in the ICS group, whereas the SCAS group showed fairly stable measurements from the third postoperative month onwards.

It is also notable from Figure 4.8 that regular topographic patterns were associated with higher cylinders in the early postoperative period. This could have been an artefact of the topographic scale used. For reasons explained in the discussion of chapter 3, we have used the absolute scale for our classification. However, if less 'sensitive' variable step sizes in the scale were utilised, this could predispose to apparently more regular patterns predominating when higher dioptric values were encountered. From Table 4.7 is also noted that the keratometric cylinder was found almost 40% higher than the refractive cylinder. Poor correlation between refraction and keratometric astigmatism has been also documented in several RK studies in the past (*Waring et al,* 1991; *Holladay & Waring,* 1992). It is thought to arise from the fact that keratometry and refraction use different plane of measurements, whilst refractive results are dependent on patients subjective responses. Furthermore some neutralisation of the corneal astigmatism may occur by either crystalline or pseudophakic lenses.

Effect of suture manipulation on astigmatism

Both techniques (suture adjustment, selective suture removal) were found to be powerful and have a similar effect in reducing astigmatism. The only difference found, was the greater effectiveness of suture adjustment as compared to selective suture removal for astigmatism greater than 3 D. Previous studies had shown that selective removal of interrupted sutures in the presence of a continuous suture, effectively reduces astigmatism. In agreement with other studies (*Binder* 1988; *Pradera et al,* 1989; *Burk et al,* 1988; *Strelow et al,* 1991), it was confirmed with the present study that single suture removal was more predictable at decreasing astigmatism than was the removal of multiple sutures at one time. In contrast, *Stainer et al.* (1982) found that the most reliable method to decrease astigmatism was the simultaneous removal of two sutures along the axis of the steepest keratometric meridian. *Burk et al.* (1988) in their study of selective suture removal based on keratometry or keratoscopy found that 18% of eyes had shown an increase. There is a striking similarity to our results (17.3% of ICS and 16.4% of SCAS eyes showed increased astigmatism after suture manipulation). In this respect, CAVK did not offer any advantage compared to keratometry and keratoscopy.

Effect of time of manipulation to final astigmatism

Healing of the donor-host interface theoretically should make astigmatic change more difficult later in the postoperative period. This should be applicable to both ICS and SCAS techniques. This study indicated that although the effect of time on suture manipulation did not differ significantly between the SCAS and ICS groups, for the SCAS a greater effect was shown when the adjustment was performed within the first 6 months. For the ICS group, time of manipulation is not important. Although *Binder* (1988) found that the change in astigmatism was less when sutures were removed more than 12 months post-PKP, he was unable to show a statistical significant effect of postoperative time on the amount of astigmatic change. His results together with the present study, question the theory that it is possible to set the cornea in a shape that is not affected by late suture manipulation. *Serdarevic et al.* (1994) in a prospective randomised clinical trial with a single surgeon, demonstrated that intraoperative adjustment of a SCAS can significantly decrease astigmatism compared to a group of patients with only postoperative adjustment (1.5 ± 0.74 D vs. 4.89 ± 1.99 D respectively), at one month postoperatively). However, when the two groups of patients were compared after suture removal at 15 months, the difference in astigmatism was not found to be significant (1.75 ± 1.04 D vs. 2.23 ± 1.72 D).

SAI and SRI changes

In agreement with our findings, *Khong et al.* (1993) in a small prospective study of 8 post-PKP keratoconic corneas showed a progressive gradual lowering of the SAI, SRI and simk indices over time following PKP. The changes noted during the first 3 months were attributed to the healing process, but changes observed between 3 and 6 months were caused also by the suture manipulation. However, the authors made the point that the SRI and SAI indices obtained at the first postoperative week may be somewhat artificially increased because of the inability of the computer to process data accurately when surfaces are very irregular.

Visual recovery

Previous studies have associated either of the techniques with rapid recovery of vision. In the *Stainer et al.* (1982) study, by exclusion of the cases with posterior segment pathology, the mean corrected VA at three months was 6/15 and at 11 to 13 months was 6/11. *Van Meter et al.* (1991) reported that patients in the SCAS group achieved optical stability an average of 7 months before ICS patients. The possible explanation given was that fewer suture manipulations may allow for earlier wound healing. In the present study it was confirmed that indeed the SCAS provides earlier optical stability (at 3 months), despite the fact that there was no difference in the average number of visits with the ICS group. It seems therefore, that rather than because of fewer visits, SCAS provided earlier visual stability because suture manipulation start much earlier in this group, as compared to the ICS eyes.

Complications

Nylon sutures can cause significant morbidity (*Acheson & Lyons,* 1991), and it is well documented that retained sutures following corneal transplantation can result in sight-threatening infections. Suture removal should be considered as soon as the wound is well healed. Exposed sutures serve as nidus for infection. Complications related to interrupted sutures and their manipulation include wound dehiscence, suture-induced irritation, vascularization and infection (*Musch et al,* 1989). With the SCAS there is a risk of iatrogenic suture breakage varying between 2.4% (*McNeill & Wessels,* 1989) to 3.8% (*Nabors et al,* 1991), allograft rejection episodes (*Nabors et al,* 1991), cheesewiring (*Temnycky et al,* 1991; *Hovding,* 1994), epithelial downgrowth and graft failure (*Karabatsas et al,* 1996b).

In the series presented here, a greater proportion (41%) of early suture loosening in the SCAS group was demonstrated. In such cases the single continuous suture should be removed, but it is well known that corneal graft wound dehiscence following early suture removal is a major risk factor for graft failure (*Williams et al,* 1993). In previous smaller series 23% (3/13) of the patients (*Serdarevic et al,* 1994) to 33.3% (4/12) of the patients (*Hovding,* 1994) with SCAS developed exposed, loose sutures several weeks to months after postoperative adjustment. *Filatov et al.* (1996) experienced 21% of loose suture within the 16 patients with SCAS. No keratoconic patients were included in that group however. In the present study it was found that keratoconic patients are at greater risk of developing a loose suture when a single continuous nylon suture is used. There is not enough scientific evidence in the literature to support an early healing response in keratoconic compared to non-keratoconic patients, and anecdotal reports are controversial on this subject. *Bradley et al.* (1993) have suggested that avascular corneas such as in keratoconus and other dystrophies, show slow regular wound healing and at least 6 months must elapse before removal of nylon sutures, whereas others (*Nabors et al,* 1991) advocate that keratoconic patients are best adjusted within the first month because they tend to be younger and the stroma may heal within two months. The findings of the present study indirectly support the hypothesis of early healing in keratoconus. There is only one laboratory study (*Zhou et al,* 1996) that has looked at the expression of wound healing and stress-related proteins in keratoconic and normal eyes as well as in other diseased corneas. In that study, expression of vimentin (an intermediate filament protein), tenascin (an extracellular matrix protein), stress-related cytokines (TGFβ, IL-1), heat shock protein 27 and ubiquitin was found to be enhanced in keratoconic corneas compared with normal human controls. However a similar enhancement was also observed in other disease conditions, and it was concluded that these are most likely non-specific response secondary to wound healing associated with different diseases. Based on the experience accumulated from our own series, we now believe that the ICS technique should be used preferentially in keratoconic eyes. The continuous 11/0 suture allows safe removal of interrupted 10/0 sutures to reduce astigmatism. In addition, when for some reason early removal of the running suture is required, this is safer in the presence of the remaining interrupted sutures. These interrupted sutures supply additional stability to the graft interface. In contrast, when a single continuous suture has to be removed, stability of the wound relies entirely on the degree of healing at the graft-host interface.

It was also shown here that loosening of the single continuous suture was associated with previous adjustment. This has also been indicated by *Hovding* (1994) and *Serdarevic et al.* (1994) who observed similar findings on patients that had postoperative suture adjustment. It is possible that nylon suture elasticity accounts for this, together with the progression of wound healing. Cheesewiring may also be implicated with manipulation of the suture loops.

Single continuous suture removal

In accordance to previous studies (*Hovding,* 1994; *McNeill & Wessels,* 1989), it was demonstrated in this study that despite the overall effect of single continuous suture removal being moderate, with some patients large unpredictable changes occur. Similar results were seen with other suturing techniques when all sutures were taken out (*Binder,* 1985; *Binder,* 1988; *Mathers et al,* 1991; *Mader et al,* 1993). In contrast, *Serdarevic et al.* (1994) found no patient having a change of more than 1.5 D after suture removal of a SCS. *Filatov et al.* (1996), comparing 16 patients with SCAS to 16 patients with ICS, 2 to 4 years post-PKP found no difference in astigmatism when all sutures were removed. The authors concluded that late suture-out astigmatism is likely to be due to factors other than the initial suture tension and subsequent suture manipulation. These results indicate that there is instability of the graft even after the first year, though these grafts were thought to be well healed and stable. In addition, they would reinforce what has already been suggested by a number of studies (*Troutman & Meltzer,* 1972; *Jensen & Maumenee,* 1974; *Troutman,* 1979; *van Rij & Waring,* 1986; *Mader et al,* 1993), that factors other than the suturing technique may play a more important role in final astigmatism after removal of all sutures. Sutures can partially mask a postoperative astigmatism, but significant astigmatic changes occur after suture loosening and removal. It is therefore important to differentiate between suture / non-suture astigmatism. Adjustment seems to mask the astigmatism from a non-suture cause by inducing a focal suture compression compensating for the non-suture factor (*Maguire,* 1993). The effect of selective removal of sutures is lost after all sutures are out and the advantage is apparent only in the first post-PKP year (*Binder,* 1985). In contrast, it seems reasonable to think however that the technique with which a graft is sutured affects not only the immediate refractive results, but also the healing process of the interface, the stability of the wound, and the final visual outcome after the removal of sutures, by influencing the healing position. As long as sutures are in place, they are probably the major factor that determine the shape of the cornea, so suture manipulation can reduce the astigmatism. Once all sutures are removed, the configuration and biomechanical stress of the wound, influenced by the shape of the donor and host corneas and by wound healing, determine the amount of astigmatism (*Binder & Waring,* 1992).

4.6. Conclusions

This study on post-PKP astigmatism has analysed the astigmatic changes of 95 patients divided into two groups (SCAS vs. ICS).

The data presented in this study suggest that postkeratoplasty astigmatism can be significantly decreased either by suture adjustment or by selective suture removal, as in the majority of cases the target of less than 3.5 D of astigmatism was achieved.

In particular there was no significant difference between the two groups in:

- the number of visits required per patient, for suture manipulation.
- the effect of suture manipulation on astigmatism (net reduction, vector change, axis change).
- astigmatism measurements (topographic, keratometric, or refractive) between the two groups at different time intervals post-PKP.
- correlation of early to late (12 months) astigmatism (poor for both groups).
- stabilisation of refraction after the sixth postoperative month and final refractive outcome (73% of ICS and 70% of SCAS eyes were within the goal of less than 3.5 D of astigmatism).
- regular / irregular patterns ratio was about 1/2 for both groups after the sixth postoperative month.
- astigmatic change effect of continuous suture removal was the same for both groups.

Few differences were elicited between the two groups, and these were:

- suture adjustment started earlier in the SCAS group, than removal of sutures in the ICS group.
- selective suture removal in the ICS group results more often in change of irregular topographic patterns to regular ones, than suture adjustment in the SCAS group does.
- there were differences in topographic patterns distribution only for the 3 month interval. In that time, more regular patterns were seen with the ICS. This difference does not hold later in the postoperative time course.
- the SAI was lower with the SCAS than with the ICS technique.
- more complications were seen with the SCAS technique. A higher complication rate was also associated with suture adjustment and keratoconus preoperative diagnosis.
- earlier stabilisation of refraction was observed in the eyes operated with the SCAS technique, but this is likely due to the discrepancy in time of beginning suture manipulation between the two groups.
- time interaction was different for the two treatment groups. The change in astigmatism is different for the two groups (at the 3 months SCAS > ICS, at 6 month SCAS ~ ICS, at 12 months SCAS < ICS).
- the effect of suture adjustment was greater during the first 6 months, but for the ICS group the selective removal of interrupted sutures is not significantly influenced by the time of sutures removal.

In summary, in our hands the ICS technique proved safer than the single adjustable suturing, and resulted in lower (non significant) astigmatism at 12 months pst-PKP.

CHAPTER 5

LATE CONTROL OF POSTKERATOPLASTY ASTIGMATISM

5.1. Introduction

In the immediate postoperative period following penetrating keratoplasty, selective suture removal or suture adjustment are methods used to reduce the astigmatism. In addition, the use of rigid contact lenses may provide successful visual results (*Genvert et al,* 1985; *Mannis et al,* 1986; *Diamond et al,* 1992). A proportion of patients however cannot be corrected with either spectacles or contact lenses. In these cases refractive surgical intervention is required. Several surgical options have been proposed for the correction of residual astigmatism, but the results remain relatively unpredictable. These surgical techniques include relaxing incisions (*Troutman & Swinger,* 1980; *Krachmer & Fenzl,* 1980; *Sugar & Kirk,* 1983; *Lavery et al,* 1985), compression sutures (*Limberg et al,* 1989), combination of relaxing incisions with compression sutures [augmented relaxing incisions] (*Troutman,* 1983; *Mandel et al,* 1987; *McCartney et al,* 1987; *Lustbader & Lemp,* 1990), the Ruiz technique [trapezoidal relaxing incision] (*Maxwell & Nordan,* 1986; *Merck et al,* 1986), and wedge resection for large amounts of cylinder (*Troutman,* 1973; *Lugo et al,* 1987). Recently (*Campos et al,* 1992; *Lazzaro et al,* 1996), excimer laser has been also used as an alternative to the surgical corrections, but substantial regression was observed which limits its effectiveness.

It has been advocated that with the use of new technological advancements in measuring the corneal contour, such as photo or videokeratoscopy, better and more predictable results would be achieved, as compared to the traditional methods (refraction and keratometry) in planning these operations (*Maguire & Bourne,* 1989b; *Cohen et al,* 1989; *McCluskey et al,* 1990; *Frangieh et al,* 1991). Others however, have questioned the cost effectiveness and superiority of CAVK over keratometry (*Strelow et al,* 1991; *Arffa,* 1992). In order for these instruments to justify their expense, they must significantly improve the diagnosis or treatment of ocular conditions. Such a conclusion can be drawn only through a prospective randomised controlled study (*Arffa,* 1988; *Frangieh et al,* 1991).

5.2. Objectives of the study

This is a prospective case-control study with randomised controls, designed to assess the role of computer assisted videokeratography in:

1) refining surgical technique, and 2) improving the predictability of surgical control of late post-PKP astigmatism. In particular the value of pre-refractive surgery videokeratography will be evaluated by;

(a) analysing the frequency and degree by which a preoperative surgical plan based upon refraction and keratometry alone was modified with the benefit of computer assisted videokeratography.

(b) comparing the outcome of videokeratography-assisted post-PKP refractive surgery with the outcome of surgery performed without the benefit of videokeratography.

(c) analysing the effect of preoperative topographic pattern to the final outcome.

5.3. Subjects & methods

5.3.1. Study population

The study population consisted of all patients undergoing surgical treatment of high postkeratoplasty astigmatism at Bristol Eye Hospital during a period of over two years. Between April 1992 and June 1994, 34 eyes (32 patients) were operated upon for disabling post-keratoplasty astigmatism. Some of these patients were referred from other Ophthalmic Units, the rest had a corneal transplant performed in this hospital sometime in the past. All patients were followed up for a year after surgery. The research protocol had received prior approval by the United Bristol Healthcare Trust Ethical Committee and written informed consent was obtained from each patient before the operation.

5.3.2. Inclusion criteria

The eligibility criteria for the patients enrolled in the study were : (1) a minimum age of 18 years, (2) a clear penetrating corneal graft performed one year or more prior to inclusion in the study, (3) all sutures had been removed for at least three months, (4) a stable post-PKP astigmatism of at least 4 D on refraction and keratometry, (5) intolerance to contact lenses or to the full cylindrical spectacle correction, and (6) absence of active corneal disease.

5.3.3. Study design [Figure 5.1]

Patients eligible for the study were randomly allocated into two groups, according to a random numbers table. Because of the controlled nature of the trial, if one patient had to be operated on both eyes, one eye was assigned into group A and the other eye into group B (controls), as suggested by *Waring* (1987b). Both groups received the same surgical treatment by means of relaxing incisions and augmentation sutures[1], but the surgical plan was based on CAVK information only in group A; in group B (controls) it was based only on refraction and keratometry. Unaided and best corrected Snellen visual acuity, manifest refraction, keratometry (10 SL/O Zeiss keratometer, Carl Zeiss, Inc.) and computer-assisted corneal topographic pictures (TMS-1, Computed Anatomy Inc, New York, NY) were obtained preoperatively for each eye.

5.3.4. Surgical treatment protocol

Group A (16 cases) represents those patients whose surgical plan was based only upon their preoperative corneal topographic picture [Figure 5.1]. These patients had an initial surgical plan (plan 1) based on the information obtained by refraction and keratometry alone, determined by a committee of at least three or more of the surgeons involved in the study. This surgical plan was recorded in the patients protocol sheet but not used for the surgical procedure. It was only recorded for later comparison with plan 2 (vide infra) in the analysis of the results. Then, the corneal topographical picture was obtained. Three videokeratography images were taken from each eye. All three images were compared to each other by monitoring the simulated keratometric readings (simk) of each examination after digital processing. Of the three images, the highest quality picture with the

[1] the term "augmentatio" is rather more appropriate that "compression", as these sutures augment the incisions rather than create effect by local tissue compression. However, in the text they are used interchangeably as the term "compression sutures" is more widely used in letterature.

minimal off-axis measurements was selected as the basis for the final surgical plan (plan 2). Using the absolute scale of the computer's software, the steep semimeridians were identified. Then the vector of each of those semimeridians was determined according to the picture. As a result there were two vectors identified, one for each semimeridian, often forming an angle between them other than 180 degrees. The same principle was applied to the flat semimeridians, which were not always at the same vector axis and usually not exactly orthogonal to the axis of the steep semimeridians. The surgical plan 2 was then drawn superimposed on the patients topographic picture. The length of the relaxing arcuate incisions was determined by the borders of the steep semimeridians and was one to three clock hours long (30 to 90 degrees). The borders of the steep semimeridians were established by the position of the small narrow band of transition dioptric power (yellow colour of the absolute scale) from hot to cool colours on the topographic map. The augmentation sutures were put in groups of one to three interrupted nylon sutures depending on the length of the flat semimeridians and the difference in dioptric power between flat and steep semimeridians [Figure 5.2]. The aim of the use of the compression sutures is to create a shift of the axis of the plus cylinder at the time of surgery, so the resulting overcorrection could be controlled by selective postoperative removal of the sutures beginning not earlier than four weeks following the operation.

Group B (controls, 15 cases) represents the patients who had their surgical plan based only upon their keratometric readings and manifest refraction [Figure 5.1]. Whenever there was a disparity in the axis between refractive and keratometric astigmatism, keratometry was taken into consideration, as corneal astigmatism is to be corrected with the procedure. Three preoperative topographic pictures were obtained and one selected on a similar manner as in group A. This picture was not printed but only kept in the computer's storage system for future comparison with a topographic picture taken at 12 months following the refractive procedure. Additionally, the examiner taking the topographical picture was excluded from the committee of surgeons deciding upon the surgical plan. For this group B (controls), a protocol of treatment was followed regarding the length of the incisions and the number of compression sutures. According to the protocol, for astigmatism measuring between 4 to 8.5 D by keratometry, paired arcuate incisions of two clock hours length each at 180 degrees apart were performed, in combination with two groups of compression sutures, each group consisting of two compression sutures, perpendicular to the vector of the relaxing incisions. For astigmatism more than 8.5 D, again a pair of two relaxing incisions -2 clock hours length each- was used, combined in this case with a total number of six compression sutures divided into two groups of three sutures [Figure 5.3].

5.3.5. Surgical technique

All procedures were performed in the operating theatre with the use of an operating microscope under sterile conditions. General or local anaesthesia was used. Five surgeons were involved in the study and operated on the cases on a random basis. They all had formal training in corneal and refractive surgery, in addition to their general ophthalmic training (either consultants ophthalmologists undertaking mainly corneal work, or corneal fellows/senior registrars); they had all performed a number of similar operations before. Throughout the study, the performed operations were monitored by the author, in order to insure adherence to protocol.

The surgical plan which was preoperatively drawn in the patients chart, was brought in theatre and lined up in the orientation of the surgeon when viewing through the microscope. Using a 12 radial keratotomy marker stained with methylene blue dye, the corneas were marked in terms of clock hours or degrees. All patients received the relaxing incisions at the graft-host interface with a diamond blade, free hand at a depth of about 90% of the corneal thickness. The attempt was to aid the opening of the wound with a toothed forceps to obtain a really deep incision up to the Descemet's level. Intraoperative pachymetry was not used as the incisions were made at the graft-host interface where the measurements are unreliable and the thickness of the tissue often varies in different areas. In the event of perforation the surgeon could elect either to observe the leak, to apply a bandage contact lens or to use a 10/0 nylon suture without tension (to be removed one week postoperatively) if the perforation was large[2]. In both groups the compression sutures material used was 9-0 Nylon. These were placed in such a way to overlap the graft-host interface on both sides, at a depth approximately 80% of the corneal thickness (*Lindstrom & Lindquist*, 1989). The sutures were tied with a slip knot, the ends were cut short and the knots were buried in the stroma. When appropriate tension of the sutures was applied, striae were observed perpendicular to the area of the sutures. Intraoperative keratometry was not used in any of the cases reported. At the conclusion of the operation the relaxing incisions were gently irrigated with a blunt cannula to flush away blood or debris.

An ocular patch was placed after the completion of the procedure with an antibiotic ointment and left for 24 hours.

5.3.6. Postoperative care and follow up protocol

Postoperatively, a combination of antibiotic and corticosteroid drops were used for two weeks, and corticosteroid drops only after epithelization of the incisions for four more weeks. The patients were examined at frequent intervals after surgery. The follow up protocol included visits at day 1, 1 month, 3 months, 6 months and 12 months after the operation, plus any extra visits as required for the manipulation of the sutures. A time 'window' of two weeks was established for the 3, 6 and 12 months visits and was accepted as providing the necessary data (*Seigel*, 1985). Selective removal of compression sutures was performed as necessary not earlier than four weeks after the operation, unless sutures became loose and caused trouble to the patients. On each follow up visit all examinations (manifest refraction, keratometry and videokeratography) were repeated for group A patients. For patients in group B, only refraction and keratometry was

[2]these sutures approximate gently the edges of the wound; they were placed superficially.

performed, with the exception of the last visit at 12 months postoperatively, when a topographic map was obtained, to compare it with the preoperative one. All patients included in the study had follow up of one year. Slit-lamp identification of tight sutures by visible stress lines in the cornea, was used for their removal in group B (controls); selective removal of tight sutures in group A was performed on the basis of the topographic map.

Uncorrected and best corrected Snellen chart visual acuity, slit lamp microscopy and retinal examination were also performed on every occasion. Clinical examination conditions and techniques were as described in section 4.3.6; type and mode of operations of the instruments used (10 SL/O Zeiss keratometer, TMS-1) have been described in chapters 2 and 3.

5.3.7. Patients analysed

Of the 34 eyes that were initially enrolled, analysis of the results includes 31 eyes of 29 patients. Three eyes had to be excluded from the analysis (2 in group A and one in group B). One patient was lost to follow up after his first follow up visit, opting not to return for further management, one patient was operated without the use of compression sutures and one patient was wrongly included in the study, having only 3 D of keratometric and topographic astigmatism (although refraction was 4.5 D).

5.3.8. Data management

Each patient had an enrolment spreadsheet in their notes with the relevant data and results were assimilated onto a computer spreadsheet (Excel).

5.3.9. Outcome evaluation

Calculation of the net astigmatic change

Astigmatism measurements and net astigmatic change were employed by : i) manifest refraction with the Jackson's cross cylinder for axis and power of cylinder, ii) algebraic difference between steep and flat axis readings with the keratometer, and iii) algebraic difference between the simulated k readings (simk) of the videokeratography.

Calculation of vector astigmatic change

The magnitude of the topographic astigmatic vector change (preoperatively to 12 months postoperatively) was calculated for each of the 31 eyes of the study, by using the method described by *Kaye et al.* (1992). Surgical effect (*K2*), surgical accuracy (*SA*) and net surgical effect in ideal axis (*K2'*) calculations [Appendix V], were performed on a spreadsheet program kindly provided by the author of the method.

Visual acuity

Analysis of unaided visual acuity (VA), as well as best corrected visual acuity (BCVA)[3] were performed by converting the Snellen notation into a decimal scale, whereby 6/6 equals 1.0 and 6/60 equals 0.10 [Appendix IV]. Numerical equivalents of 2/60, 3/60 were also used for VA less than 6/60, whereas visual acuity described as "counting fingers" (CF) was substituted with a numerical equivalent of 1/60, as described and used in similar previous studies (*Bradley et al,* 1993; *Vail et al,* 1994). The fractions were then modelled on the logarithmic scale [Appendix IV]. Finally, the geometric rather than the arithmetic mean of VA was considered as suggested by *Holladay & Prager* (1991)[4].

Topographic patterns analysis

The classification system proposed in chapter 3, was used for the qualitative analysis of the topographic maps.

5.3.10. Statistical analysis

Treatment groups comparisons were performed using different statistical tests according to the examined factor. Comparisons of categorical data was performed using the Fisher's exact test. Changes in astigmatism from baseline were compared for each follow up visit using the Wilcoxon's rank test for non-parametric data. The two treatment groups were compared at each visit using one-way two-tailed ANOVA test. To determine whether any demographic or clinical factors were

[3] defined as VA with spectacles or contact lenses

[4] this was calcualted by taking the logarithm of each of the sample values, determining the average of the logarithmic values, then taking the antilogarithm of this average.

associated with the amount of astigmatic change, single factor one-way ANOVA was used to compare mean topographic astigmatic change among different categories of factors. All statistical analyses were personally performed using SPSS for Windows on an IBM compatible computer. Significance was defined as $p < 0.05$ for all tests. For non-parametric data, mean (average) and SEM values were used.

5.4. Results

5.4.1. Preoperative groups comparisons / baseline data

Data regarding the original pathology, keratoplasty surgical technique and demographic data for the two groups are summarised in detail in Tables 5.1 and 5.2. In group A, 10 patients had their operation under local anesthetic and 6 patients under general anesthesia. In group B, 9 patients received treatment under local anesthesia and 6 patients under general anesthesia. No significant differences between the two treatment groups were seen at baseline. The two groups were well matched for mean preoperative astigmatism as well, as none of the differences was statistically significant. Topographic astigmatism was 8.00 ± 0.92 D and 9.44 ± 0.84 (p=0.262) for group A and B respectively. The values of preoperative keratometric astigmatism (D) were 8.60 ± 0.89 and 10.21 ± 0.94 (p=0.224) respectively; preoperative refractive cylinder was measured 8.51 ± 0.99 and 8.93 ± 0.65 (p=0.731) for groups A and B respectively.

5.4.2. Intraoperative parameters

In group A, 14 eyes had two arcuate keratotomies, whereas in 2 eyes only one arcuate keratotomy was performed, according to the topographic map. The length of the keratotomies ranged from 30 to 90 degrees (1 to 3 clock hours). The number of compression sutures differed from 0 to 3 on each flat semimeridian. In group B all eyes had paired arcuate keratotomies of 60 degrees (2 clock hours) each. Twenty-three of the 31 procedures (74.2%) were completed without intraoperative complications, whereas in 2 eyes of group A and 6 eyes of group B

($p<.001$) intraoperative perforation occurred during the relaxing keratotomy. Both cases of intraoperative leak in group A were treated as micro-perforations with a bandage contact lens and no postoperative sequelae; in group B 3 cases had micro-perforations ($p=0.467$), and 3 cases were big enough perforations to require the placement of 10/0 nylon sutures at the site of arcuate keratotomies ($p=0.101$). In one of these cases a persistent aqueous leak was developed despite the placement of sutures and was eventually successfully treated with the use of cyanoacrylate glue. A marked regression of the surgical effect was observed in this case (*Karabatsas & Easty*, 1997).

5.4.3. The influence of topographic map on surgical plan

For group A, the preliminary choice of incisions axis and length, as well as number and position of compression sutures to be placed on the basis of keratometry and refraction alone (plan 1), was changed in all 16 cases, when information from the topographic map was added (plan 2). The axis of the first relaxing keratotomy cut, was different by that in plan 1, by a mean of 11 degrees (range, 0 to 35 degrees). On two occasions, the axis was exactly the same for the two surgical plans. The axis of the second relaxing keratotomy cut differed from that of plan 1 by a mean of 14 degrees (range, 0 to 35 degrees). In only one case this difference was 0 degrees, whereas on two eyes no second cut was required according to the topographic map. In 4/16 eyes the paired incisions length was 2 hours each, as it would have been if no topographic information was used, but for the rest of the cases the cut lengths varied accordingly from 0 to 3 hours. The total length of incisions that should have been performed if plan 1 was followed on all 16 eyes of group A, this would have been 64 hours [16 x (2+2)]. Instead, by following plan 2, a total length of 63 hours was eventually performed.

The number of compression sutures that should be used if plan 1 was followed for group A, should be (3+3) in 6 cases and (2+2) in 10 eyes. In only two cases this did not change after the topographic map review. In 3 cases, no pairs were used; sutures were placed instead only on one side, because of topographic asymmetry.

The total number of sutures used was 67 (mean: 4.2 sutures per case); if plan 1 was to be followed this number would be 76 (mean: 4.7 sutures per case).

5.4.4. Topographic astigmatism

Table 5.3 shows the statistical data for topographic astigmatism (simk, D). Both treatment groups exhibited significant reduction of topographic astigmatism at each follow up visit except on the one month visit, before compression sutures manipulation started. At 12 months following surgery, both groups resulted in a significant net reduction of baseline simk astigmatism ($p=0.0019$ for group A; $p=0.0012$ for group B). The mean net simk reduction for group A was 47%, and for group B was 40.7%. However, this reduction was not significantly different between the two groups ($p=0.950$). The two groups showed no significant difference on their 12 months mean topographic astigmatism measurements (4.24 ± 0.71 vs. 5.60 ± 0.51 for group A and B respectively, $p=0.139$). In group A, at 12 months 15/16 eyes had lower topographic astigmatism than preoperatively (range, -0.6 to -15.8 D). In one case however, postoperative astigmatism was higher than preoperative by 2.9 D (simk). In group B respectively, on two eyes postoperative astigmatism measured higher than preoperatively (by 0.4 and 1.4 D). For the rest of the cases the range of improvement was from -1.9 to -8.3 D [Figure 5.4].

5.4.5. Vector analysis of topographic astigmatism (simk, preoperatively vs. 12 months postoperatively)

The vector astigmatic calculations, based on the method described by *Kaye et al.* (1992), are displayed in Table 5.4. The average vector astigmatic effect against the average preoperative measurements for both groups are also shown in Figure 5.5. The average vector surgical effect (K2) for group A, was 90.7% of the preoperative average astigmatism; for group B the surgical effect was lower (70.1% of the preoperative value), but the difference between the two groups was not significant. Surgical accuracy (SA) for the two groups was also calculated. This indicates how accurate the surgical effect was in the intended axis. These values vary from +1 (best) to -0.5 (worse, at 90 degrees off to the plan). If for example the result is 0.88, this means 88% of the effect was on the correct axis. For both groups the SA was not very good, but similar (0.55 and 0.46 for groups A and B respectively, p=0.26).

The net surgical effect in the ideal axis (K2') also was very similar (p=0.62) between the two groups (6.43 ± 5.12 for group A, 5.66 ± 2.93 for group B).

Finally, the attempted axis vs. the axis achieved, showed that in group A 6 eyes had off axis more than 25 degrees, and 4 eyes in group B [Figure 5.6].

5.4.6. Keratometric astigmatism

The keratometric astigmatism changes are displayed in Table 5.5. For both groups refractive keratotomies with compression sutures resulted in significant reduction of keratometric readings from the third to the twelfth postoperative month. The average net astigmatism at 12 months was significantly lower in group A (p=0.035), although the net change to the baseline astigmatism was not significantly different between the two groups (p=0.720). However, group A also showed a larger percentage of preoperative astigmatism correction (58%) compared to group B (43.5%). For most of the eyes, the keratometric astigmatism was slightly higher than the refractive astigmatism.

5.4.7. Refractive astigmatism

The percentage of eyes achieving an astigmatic correction within 4.00 DC at the 1 year examination was higher in the group A. In this group, only one eye (6.25%) was left with more than 4.00 DC astigmatism as compared to 10 eyes (66.7%) of the group B [Figure 5.7]. Refractive astigmatism achieved significance between the two treatment groups at 12 months post-surgery, with group A showing lower mean astigmatism [Table 5.6]. Reduction of refractive astigmatism (range, 1.5 to 19.25 DC) was seen in all 16 eyes of group A, which demonstrated a mean reduction of 72.5% to the baseline preoperative measurements. Astigmatic reduction was also seen in 14/15 eyes of group B (range, 0.25 to 5.75 DC). One eye in this group showed a 0.5 DC deterioration at 12 months. In this group the mean reduction of refractive astigmatism was 45.3% ($p=0.088$). No differences between the two groups was seen on the mode of treatment of the residual refractive error at 12 months. Four patients in group A and 5 patients in group B previously intolerant to contact lenses, were treated with rigid gas permeable contact lenses postoperatively, the rest (12 eyes in group A and 10 in group B) with glasses.

5.4.8. Topographic patterns

A total of 62 topographic maps (31 preoperative and 31 postoperative, at 12 months) were reviewed by two examiners and classified according to the methods described in chapter 3. Initial agreement was achieved in 55 maps (88.7%), whereas after a second review there was agreement for all topographic maps. Of the 31 eyes, 22 eyes (71%) showed regular astigmatic patterns preoperatively. Postoperative examination at 12 months, revealed the distribution showed in Table 5.7. In group A, the effect of surgery was an increase of the non-astigmatic patterns, decrease of the pooled regular patterns, and increase of the pooled irregular patterns. However, numbers were too small to achieve any statistically significant variation from the preoperative baseline (all p values NS with Fisher's exact test). Numbers were small in group B too, for statistical significance. Irrespective of treatment plan, surgery has resulted in significant reduction of the regular topographic patterns from 71% to 48.4% ($p<0.001$), and respectively increase of the irregular patterns from 29% to 42% ($p=0.213$). Surgical correction also produced non-astigmatic topographic patterns in 3 cases (9.6%, $p=0.118$). A reduction of the PABT pattern was the only significant sub-group change observed ($p<0.001$).

5.4.9. SRI, SAI changes

No significant treatment differences were found either within treatment groups, or at each follow up visit between groups, for both SAI and SRI. For group A, the SAI (mean $\pm$ SEM) preoperatively was 1.05 ± 0.13 and at 12 months post-surgery 1.13 ± 0.23. For group B the SAI values were 0.96 ± 0.18 and 0.88 ± 0.14

respectively. For SRI, the changes were also minimal (from 1.44 ± 0.72 to 1.18 ± 1.24 for group A, and from 1.64 ± 0.54 to 1.52 ± 1.46 for group B).

5.4.10. Visual acuity

For the group A, the average calculated preoperative unaided Snellen notation[5] was a 6/66 equivalent. This was significantly improved (p=0.02) after surgery to an equivalent mean Snellen acuity of 6/39. For the group B, the average unaided preoperative Snellen equivalent visual acuity was as low as 6/128 and this was significantly improved (p=0.0003) after surgery to an average Snellen equivalent of 6/46. One eye in group B had worse unaided visual acuity after surgery as compared to none in group A, but the two groups showed no significant difference (p=0.57) in mean postoperative unaided logMAR converted visual acuity. Figure 5.8 illustrates the unaided visual acuity change with surgery for both groups.

In group A keratorefractive surgery resulted in a significant improvement of BCVA from a mean of 6/11 before surgery to 6/8.2 mean Snellen equivalent after surgery (p=0.005). In this group A, 10 patients had improved BCVA postoperatively of one Snellen line or more, 5 had no change, but one patient lost one line of BCVA after surgery. For group B, surgery did not change significantly the mean BCVA (6/7.9 preoperatively, 6/8.2 postoperatively, p=0.70). Although postoperative mean BCVA did not differ significantly between the two groups (p=0.99), there were only 4/15 patients of group B that had better Snellen VA postoperatively by one line or more (p<0.0001 to group A). There were also 8 patients in group B that did not show any change to Snellen BCVA with surgery (p=0.189 to group A); there was one patient who lost one Snellen line, whereas two patients lost two lines (p=0.225 to group A). Figure 5.9 shows the changes in BCVA for the two groups. Similar visual acuity results for the two groups comparison were seen when 4 cases (two on each group) were excluded, because

[5]The geometric mean was calculated (by taking the antilogarithm of the average of the logarithm values); the resultant converted to Snellen notation for reporting the mean acuity. Statistical comparisons were performed for the geometric means between and within groups.

of retinal pathology (one case with high myopic fundus changes, one patient with severe age related macular degeneration) and amblyopia (two eyes).

5.4.11. Factors associated with astigmatic change

The effect of different other factors affecting the outcome was also examined with one-way ANOVA for the mean reduction of topographic astigmatism at 12 months from the preoperative baseline. The following categories of factors examined were found to have no significant influence to outcome: treatment group (p=0.9007, group A vs. B), patient's sex (p=0.2604), patient's age (p=0.7016, dichotomised at the mean age of 53 yr.), preoperative diagnosis (p=0.1497, KC vs. non KC), surgeon code (p=0.3383), surgeon's level (p=0.1344 for senior vs. junior surgeon), intraoperative complications (p=0.6469, for no complications, micro-perforations, macro-perforations), corneal shape (p=0.1173, for prolate, oblate, mixed).

Factors that were found to be significantly related to outcome were: Previous refractive surgery was found to be related with a lower astigmatic reduction (p=0.045). Preoperative astigmatic pattern was also found to be related to surgical outcome. Regular astigmatic patterns showed a greater reduction of astigmatism than irregular patterns (p=0.0082). Sub-classification of the pooled groups also revealed significant influence on the outcome (p=0.000). Further statistical testing (with Bonferroni modified test) indicated that the OSBT and the PSBT patterns were associated with significantly greater astigmatism reduction.

5.4.12. Example

A case example is illustrated in Figure 5.10.

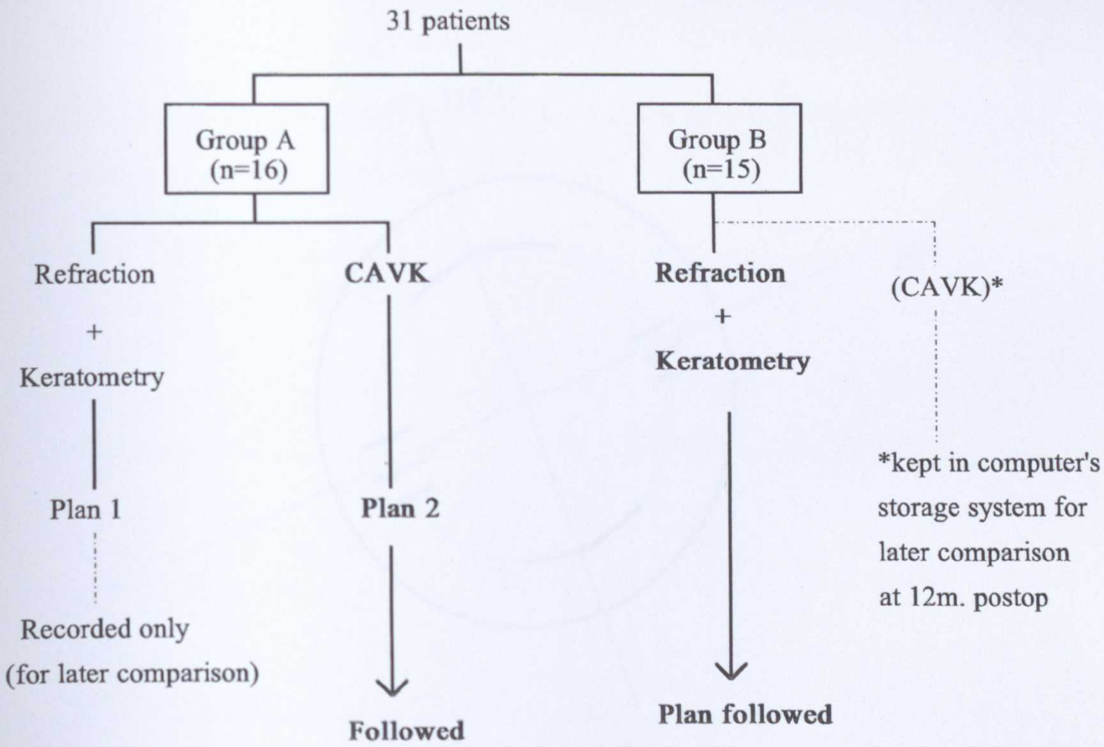

Figure 5.1 : Study design

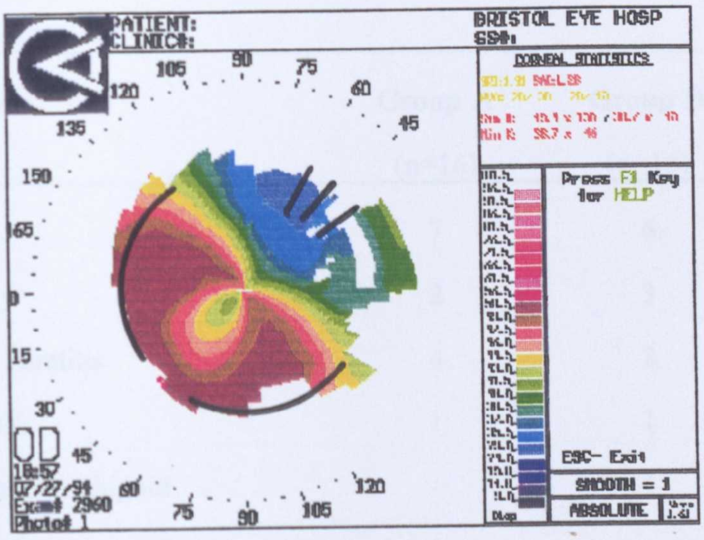

Figure 5.2: Example of the surgical plan followed, based on the topographic map in a patient of group A.

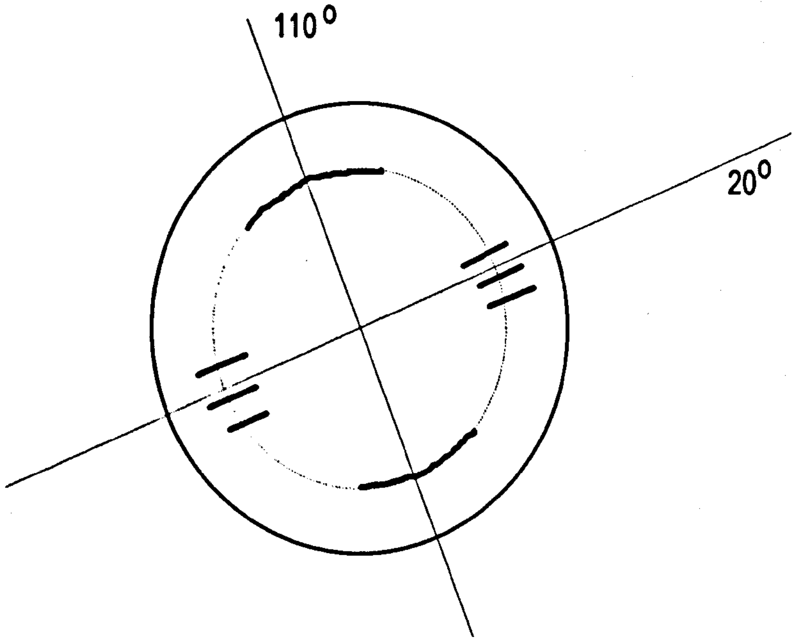

Figure 5.3: Example of the surgical plan followed on a patient of group B, with refraction of -3.50 / +9.00 x 120 and keratometric readings of 41.20 @ 20 / 50.40 @ 110.

TABLE 5.1 : Distribution of prekeratoplasty corneal pathology

Corneal disease	Group A (n=16)	Group B (n=15)	Total (n=31)
Keratoconus	7	6	13
Fuch's dystrophy	2	3	5
Herpes simplex keratitis	4	2	6
Pseudophakic BK	1	1	2
Ocular cicatricial pemphigoid	-	1	1
Granular dystrophy	1	-	1
Congenital endothelial dystrophy	-	2	2
Interstitial keratitis	1	-	1

TABLE 5.2 : Demographic data for the 31 eyes undergoing surgical correction of high post-PKP astigmatism

		Group A (n=16)	Group B (n=15)	Total (n=31)
Mean age (years)		52.3 (23-84)	54(23-84)	
Sex	males	7	9	16
	females	9	6	15
Eye	Right	7	4	11
	Left	9	11	20
Size difference host/donor	0 mm	-	2	2
	0.25 mm	10	6	16
	0.50 mm	3	5	8
	unknown	3	2	5
Suturing technique for PKP	SCS	5	3	8
	CC	9	7	16
	ICS	-	3	3
	I x 16	-	1	1
	unknown	2	1	3
Previous refractive surgery	No	11	13	24
	Yes	5	2	7
Mean time since PKP (months)		39 (16-60)	47.4(12-191)	
Mean time since last sutures removal (months)		22.5 (3-54)	19.3 (3-104)	

SCS : single continuous suture; CC : double continuous suture; ICS : interrupted and continuous suture; I x16 : sixteen interrupted sutures

TABLE 5.3 : Statistical data for topographic astigmatism (simk, D)

Treatment			Month 0	1	3	7	12
Group A		average	8.00	8.98	4.97	4.66	4.24
		SEM	0.92	1.84	0.77	0.65	0.71
		Δ astigmatism	-	0.97	-3.03	-3.34	-3.76
		SE of Δ astigmatism	-	1.73	1.13	0.97	0.99
	p value	Wilcoxon test	-	0.641	0.017	0.007	0.0019
Group B		average	9.44	-	-	-	5.60
		SEM	0.84	-	-	-	0.51
		Δ astigmatism	-	-	-	-	-3.84
		SE of Δ astigmatism	-	-	-	-	0.70
	p value	Wilcoxon test	-	-	-	-	0.0012
	p value	one-way ANOVA	0.262	-	-	-	0.139
	p value	one-way ANOVA for the Δ astigmatism	-	-	-	-	0.950

TABLE 5.4 : Surgically induced vectorial astigmatism (average ± SEM)

	Group A	Group B	*p* value
Preoperative astigmatism	8.00 ± 0.92	9.44 ± 0.84	
Surgical effect *(K2)*	7.26 ± 5.24	6.62 ± 2.68	0.68
Surgical accuracy *(SA)*	0.55 ± 0.24	0.46 ± 0.21	0.26
Net K2 in ideal axis *(K2')*	6.43 ± 5.12	5.66 ± 2.93	0.62

TABLE 5.5 : Statistical data for keratometric astigmatism (D)

Treatment			Month				
			0	1	3	7	12
Group A		average	8.60	8.65	4.78	4.82	3.60
		SEM	0.89	1.81	0.77	0.78	0.81
		Δ astigmatism	-	0.05	-3.81	-3.77	-4.99
		SE of Δ astigmatism	-	1.83	1.07	1.07	1.16
	p value	Wilcoxon test	-	0.2775	0.0052	0.0038	0.0023
Group B		average	10.21	11.65	5.51	5.88	5.77
		SEM	0.94	1.88	0.73	0.70	0.52
		Δ astigmatism	-	1.43	-4.69	-4.33	-4.44
		SE of Δ astigmatism	-	1.94	1.13	0.98	0.95
	p value	Wilcoxon test	-	0.5701	0.0012	0.0010	0.0038
	p value	one-way ANOVA	0.224	0.262	0.498	0.327	0.035*
	p value	one-way ANOVA for Δ astigmatism	-	0.609	0.575	0.706	0.720

* indicates statistical significance between the two groups of treatment

TABLE 5.6 : Statistical data for refractive astigmatism (cyl D)

Treatment		Month 0	1	3	7	12
Group A	average	8.51	6.17	4.01	2.95	2.34
	SEM	0.99	1.15	0.56	0.48	0.37
	Δ astigmatism	-	-2.34	-4.50	-5.56	-6.17
	SE of Δ astigmatism	-	1.22	0.93	1.17	1.05
p value	Wilcoxon test	-	0.0280	0.0011	0.0006	0.0084
Group B	average	8.93	9.15	4.13	4.21	4.88
	SEM	0.65	1.54	0.67	0.61	0.52
	Δ astigmatism	-	0.21	-4.80	-4.71	-4.05
	SE of Δ astigmatism	-	1.43	0.80	0.71	0.52
p value	Wilcoxon test	-	0.7764	0.0014	0.0008	0.0010
p value	one-way ANOVA	0.731	0.130	0.894	0.115	0.00038*
p value	one-way ANOVA for Δ astigmatism	-	0.182	0.810	0.550	0.088

* indicates statistical significance between the two groups

TABLE 5.7 : Distribution of the qualitative videokeratographic patterns before and 12 months after surgical correction of astigmatism.

	Preop			12 months postop		
Topographic pattern	Group A (n:16)	Group B (n:15)	Total (n: 31)	Group A (n: 16)	Group B (n:15)	Total (n: 31)
Non astigmatic	-	-	-	**2 (12.5%)**	**1 (6.6%)**	**3 (9.6%)**
PSBT	2	2	4	-	1	1
PABT	3	4	7	-	2	2
OSBT	1	-	1	1	1	2
OABT	3	7	10	4	6	10
Regular	**9 (56.2%)**	**13 (86.6%)**	**22 (71%)**	**5 (31.2%)**	**10 (66.7%)**	**15 (48.4%)**
PI	-	1	1	1	-	1
OI	1	1	2	-	2	2
mixed	4	-	4	3	-	3
horseshoe	-	-	-	1	-	1
triple	-	-	-	-	1	1
SF	-	-	-	3	-	3
LS	-	-	-	-	1	1
unclassified	2	-	2	1	-	1
Irregular	**7 (43.8%)**	**2 (13.4%)**	**9 (29%)**	**9 (56.2%)**	**4 (26.7%)**	**13 (42%)**

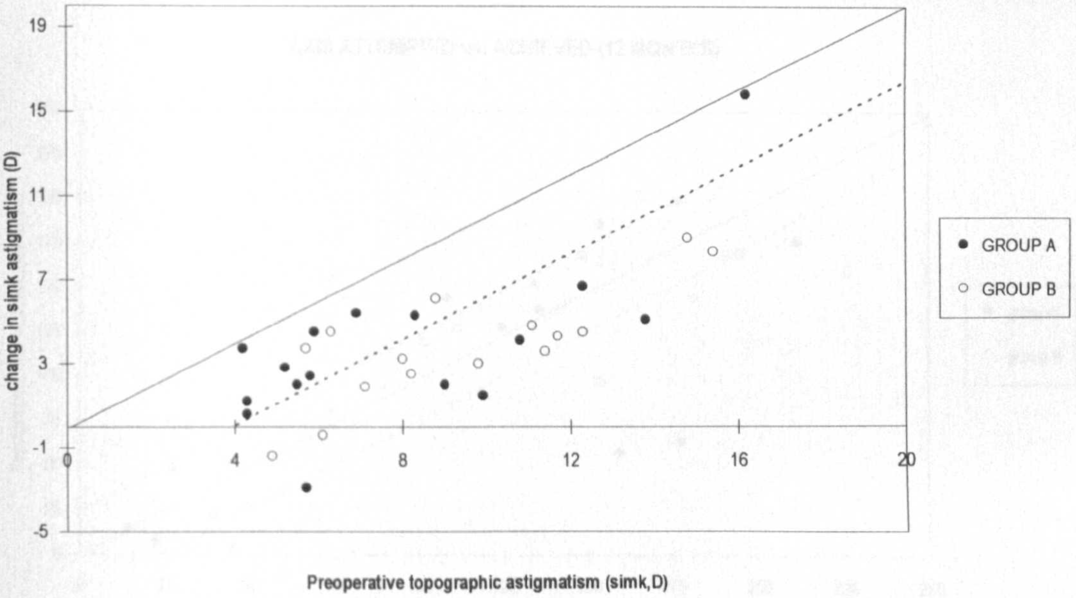

Figure 5.4: Topographic astigmatic change at one year after refractive surgery. The intersecting diagonal line indicates the ideal line of total elimination of astigmatism by surgery. Values falling within the diagonal and the dotted lines are eyes ended up with less than 4 D of postoperative topographic astigmatism. Negative values on the y axis and respectively eyes falling below the x axis (n=3), indicate worse astigmatism postoperatively than preoperatively.

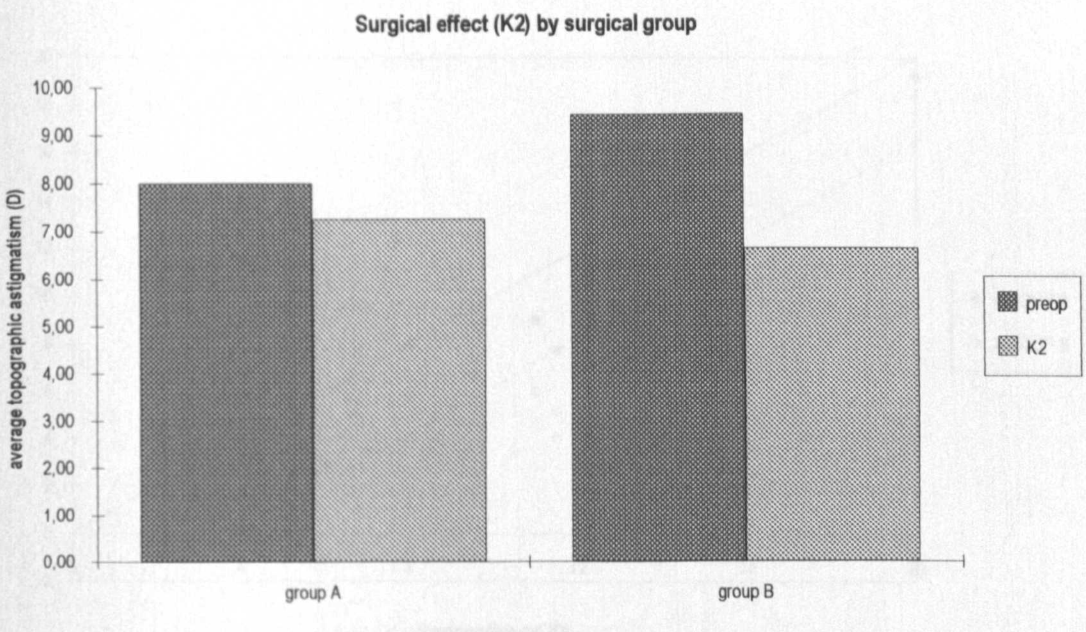

Figure 5.5 : Surgical effect (K2) for the two groups, compared to average preoperative astigmatism.

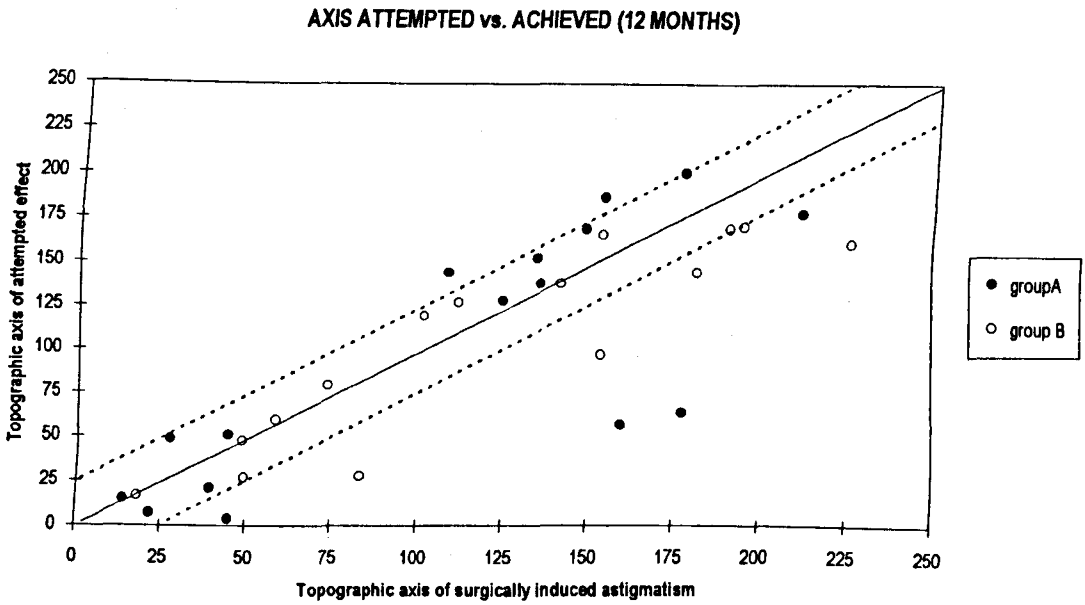

Figure 5.6 : Scatterplot comparing the axis of attempted astigmatic correction (Y-axis) to the axis of surgically induced astigmatism (X-axis). Oblique line indicates the line of equality between the two.

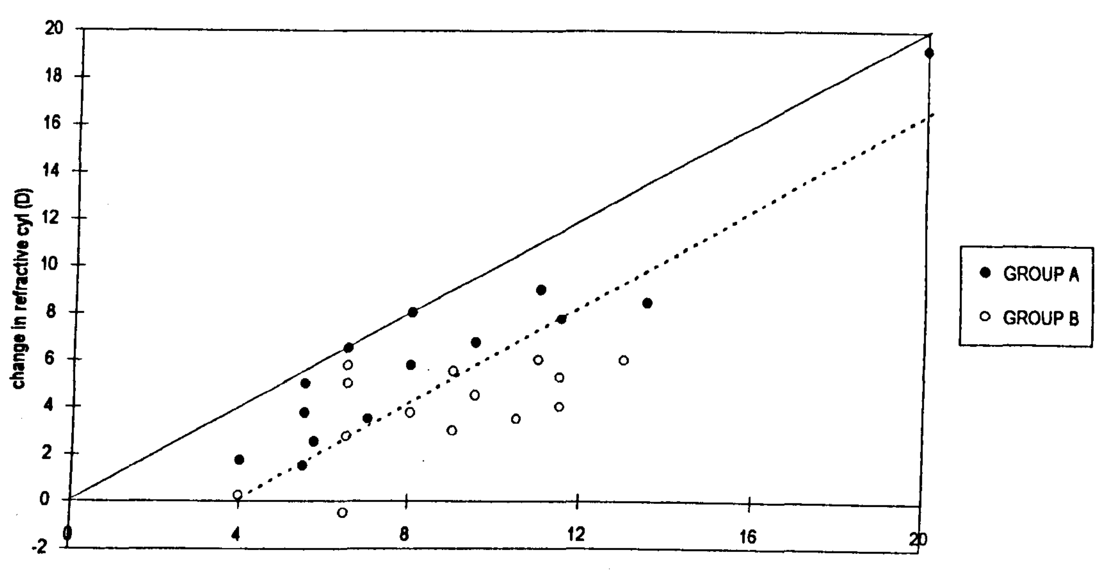

__Figure 5.7__ : Preoperative refractive cylinder (DC) vs. change in refractive cylinder with surgery (irrespective of axis). The intersecting diagonal line indicates the ideal line of total elimination of refractive astigmatism, by surgery. Eyes falling within the diagonal line and the dashed line indicate magnitude of residual postoperative refractive astigmatism less than 4 DC. Eyes falling below the x-axis (n=1), indicate higher astigmatism postoperatively than preoperatively.

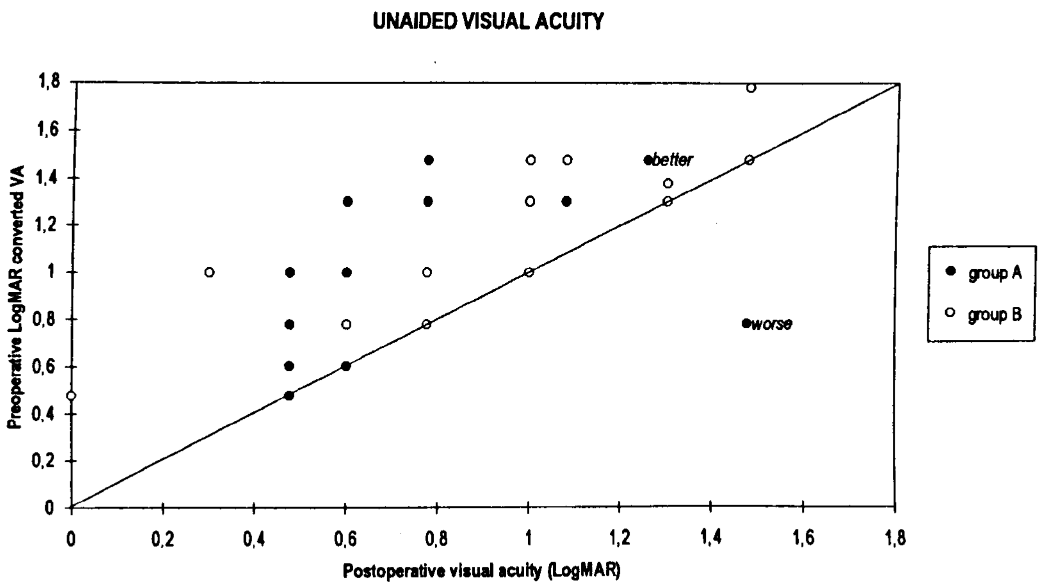

Figure 5.8 : Scatterplot of unaided visual acuity preoperatively vs. postoperatively for the two treatment groups

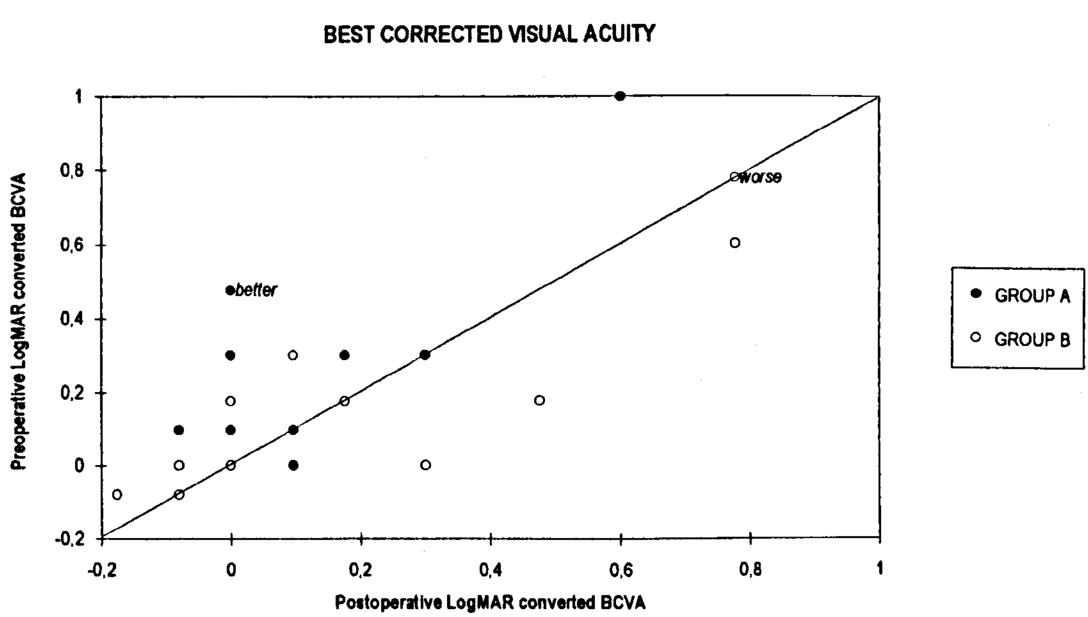

Figure 5.9 : Scatterplot of best corrected visual acuity preoperatively vs. at 12 months postoperatively for the two treatment groups

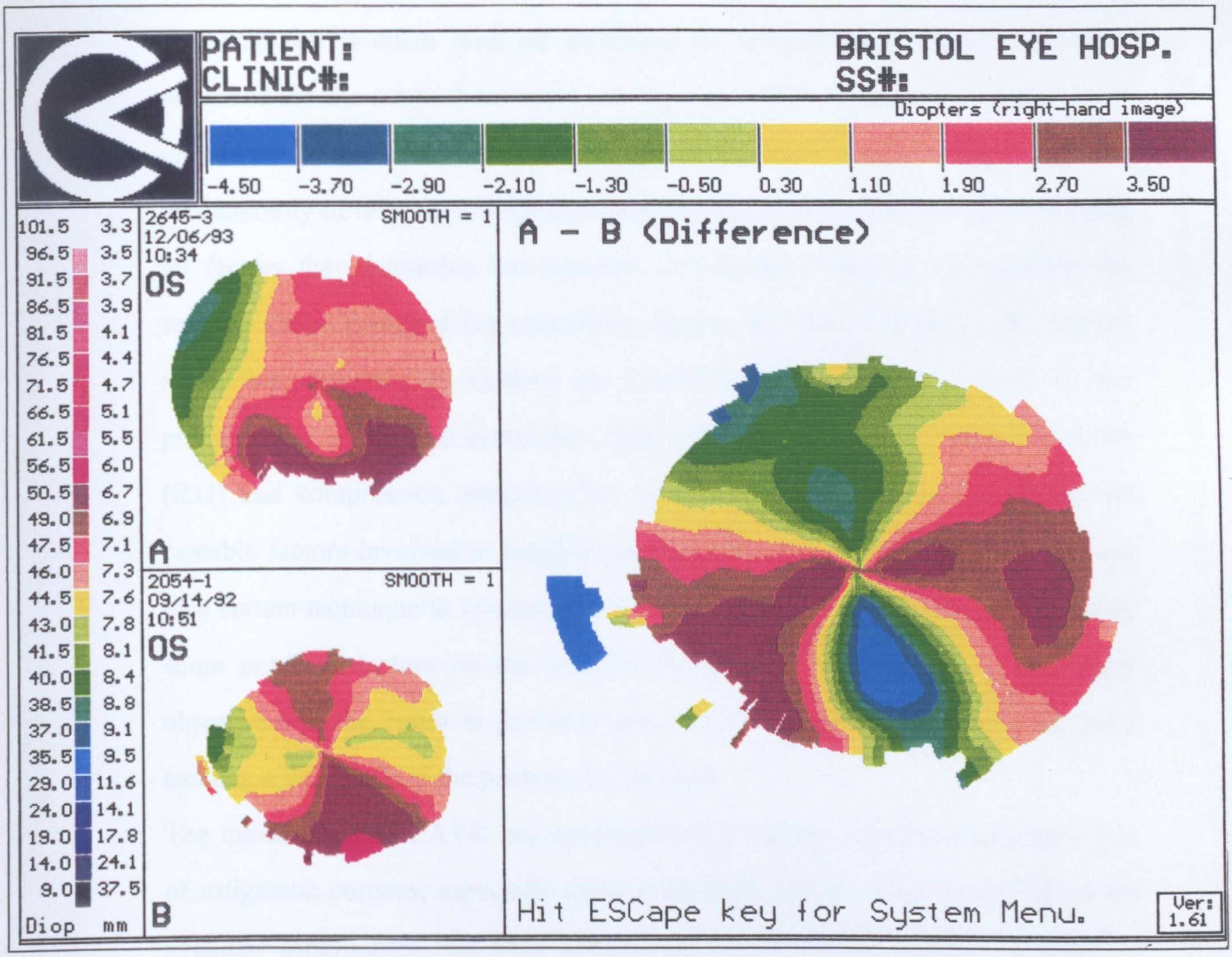

Figure 5.10 : Example illustrating the effect of relaxing keratotomy and compression sutures as a differential display map on a patient of group A. The preoperative (B) and 14 months postoperative (A) topographic maps are shown on the left side, with the dioptric values expressed by the left hand colour scale. The differential map (A-B) indicates that the effect of surgery was on the correct direction, by (a) flattening the inferior steep semimeridian, (b) flattening the superior steep semimeridian to a lesser degree, (c) steepening the two horizontal flat semimeridians. As a result, the cornea now shows a more regular pattern with less astigmatism.

5.5. Discussion

The common problem with all incisional or compressive surgical techniques described for the surgical correction of high post-PKP astigmatism (*vide* general introduction), has been the poor predictability and accuracy. Generally, the predictability of refractive surgical procedures can be improved by: (a) identifying all factors that determine the outcome of refractive surgery, (b) refining the surgical techniques, and (c) controlling the corneal wound healing. The present study was designed to explore the potential contribution of CAVK to the predictability of surgical correction of post-PKP by means of relaxing incisions (RxI) and compression sutures (CS). The study was not meant to identify all possible factors involved in surgical predictability, or to look at the effectiveness of a certain technique in comparison to other methods. However, the influence of some potential factors on the surgical outcome, was assessed as a secondary objective. As the result is probably affected by the surgical method, the same technique was used in the present clinical trial.

The introduction of CAVK has emphasised the radially asymmetrical asphericity of astigmatic corneas, especially those after PKP, and has also demonstrated the irregular astigmatism that these corneas present. It seems therefore sensible to think that asymmetric astigmatism would theoretically require asymmetric surgical correction. Planning asymmetric astigmatic surgery however, can only be done with the help of CAVK and careful studies are needed to compare this to standard symmetric surgery based on keratometry or refraction.

Several surgical nomograms exist for the correction of naturally occurring regular astigmatism. These are based on both cadaver eye models and pilot clinical trials. In an eye bank eye model of arcuate incisions *Duffey et al.* (1988), showed that there is a linear relationship for the diameter of the surgical zone (the smaller the zone the greater the effect) and the length of the incision (the longer the incision the greater the effect). An increased flattening in the incised meridian of approximately 2.00 D for every 30° of lengthening of the incision was observed.

For the 7 mm zone where most of the procedures in our study were performed, paired arcuate incisions of 60° (2 hours) were found to cause a 6.45 ± 1.37 D of vector surgically induced astigmatic change. *Tripoli et al.* (1987) also studied the effect of relaxing keratotomies in different zones and concluded that a 7 mm optic zone may be the most clinically useful to modify corneal topography. In a previous cadaver study (*Lundergan & Rowsey,* 1985), relaxing incisions at the 7.5 mm optic zone had demonstrated a wide range of effects on corneal astigmatism. The effect ranged from 0.58 D for a single clock hour incision, to 5.93 D for a unilateral 3 clock hour incision. Symmetrical relaxing incisions placed 180° apart produced 0.78 D of astigmatic change for 1 clock hour incisions, but as much as 13.97 D of change for symmetrical 3 clock hour incisions. A marked disparity between the magnitude of change following symmetrical 2 and 3 clock hour incisions in eye bank eyes indicated a narrow surgical "safe" zone. This is one of the main reasons it was decided to use paired two hours relaxing incisions in all patients of the control group B in the present study, and to vary only the number of compression sutures that enhance the effect. For group A, it was decided to follow the topographic map, but not to exceed 90° (3 hours) incision, in accordance to previous reports (*Duffey et al,* 1988; *Lindstrom & Lindquist,* 1989; *Lindstrom,* 1994). Although others (*McCartney et al,* 1987) have reported success with incisions up to 120°, we believe there is a limited length of RxI that can be performed in post-PKP eyes without facing different problems (dehiscence risk, instability of wound, excessive wound gape etc). Joining the two incisions that approach from different directions should also be avoided, since this can result in a raised wound edge and a non-healing epithelial defect with potential complications (*Olson,* 1988). Generally speaking correlation of a cadaver model to clinical practice is not perfect (*Duffey et al,* 1988), although for trapezoidal astigmatic keratotomy this correlation has been found quite good (*Merck et al,* 1986). Authorities in the field of refractive surgery suggest the non applicability of published RK and AK nomograms or regression formulas as regards their use in the treatment of post-PKP astigmatism (*Lindstrom,* 1994). Although it can be postulated that the same factors previously found (*Price et al,* 1995) to affect the outcome of refractive keratotomy in normal corneas (i.e., number and length of incisions, size of optical zone, patient age and gender, preoperative keratometric readings), can probably also affect the outcome of refractive keratotomy on grafts, the exact influence of this remains yet to be quantified for post-PKP eyes through large series. Any congruous tissue transmits forces of relaxation or tension uniformly unless impaired in some way. If there is any interference by a barrier or discontinuity, this uniformity will be interrupted. Tissues incongruous to the corneal stroma are the limbus and any scars present in the cornea (*Thornton,* 1994). The graft wound interface has a similar effect.

Graft refractive surgery has been described in many different forms, but the surgery in the present study was confined to relaxing incisions with compression sutures for both treatment groups. *Agapitos et al.* (1989) compared the clinical results from 6 different techniques of astigmatic keratotomy in eyes with naturally occurring, post cataract and post-PKP astigmatism and came to the conclusion that intraincisional relaxing incisions with or without compression sutures, seem to show greater predictability than straight or arcuate astigmatic keratotomies. Relaxing incisions with or without compression sutures have been the most popular technique for the correction of post-PKP astigmatism. A number of reports have demonstrated mean net reduction of astigmatism after PKP from 31.6% to 77% using this technique [Table 5.8]. Different incision techniques (variations in location, length, depth, number and pattern of incisions and the use of compression sutures), optical zones, follow-up periods and patient selection criteria, make direct comparison of results of different studies impossible. Although the use of compression sutures is thought to enhance the results, no prospective randomised trial comparing relaxing incisions with and without compression sutures has been done.

TABLE 5.8 : Previous studies with relaxing incisions with or without compression sutures on post-PKP eyes

Study	R /P	No. eyes	Technique	surgical details	surgery planned on ...	No. surgeons	Preop astigmatism (mean, SD)	Postop astigmatism	Net mean astigmatism decrease	mean % decrease	F/U mo.
Troutman & Swinger,1980	R	4	RxI	RxI 60-80^{o}	Km	?	11.18 (7-13.25)	2.81 (2-3)	8.37 (5-10.25)	**74,8**	<4
Krachmer & Fenzl,1980	R	14	RxI	interface, 2x2 hours	Km	?	9.57 ± 1.87 (7-12.25)	5.05 ± 2.5 (1.5-10.25)	4.52 ± 1.68 (2-7.75)	**47,2**	8.25 (2-31)
Sugar & Kirk,1983	R	15	RxI	interface, 2x3 hours	Km	?	12.47 ± 3.11 (8.5-18)	4.95 ± 2 (2-8.5)	7.53 ± 3.13 (2.5-11.5)	**60,3**	3 weeks to 7 mo.
Lavery et al,1985	R	17	variable (most RxI)	interface, 2x3 hrs	Km	2	11.13 ± 4.24 (6-22.63)	7.60 ± 4.63 (1.25-22.63)	3,52 ± 5.52 (-9 to 15.13)	**31,6**	3-8 weeks
Mandel et al,1987	P	19	RxI + CS	interface, RxI 2x2 hrs CS 2x3	Km	?	9.73 ± 2.83 (4.5-14.5)	3.17 ± 2.2 (0-7)	6.56 ± 3 (1-11)	**67,4**	6-9
McCartney et al,1987	R	11	RxI + CS	graft, RxI 2-3 hrs CS 2x1	Km	?	11.68 (6.5-19)	3.91 (1.5-9)	7.77 (5-12.5)	**66,5**	13.5 (6-21)
Maguire & Bourne,1989b	R	5	RxI	variable	P/ky	5	7.92 ± 1.2 (6.13-9)	4.82 ± 1.26 (2.63-5.87)	3.1± 0.63 (2.13-3.75)	**39,1**	2-3
Cohen et al,1989	P	7	RxI	interface, 50-80^{o} pachymetry	P/ky cadaver eyes study	?	9.27 ± 2.14 (4.5-10.88)	2.75 ± 2.25 (0-6.12)	6.52 ± 2.71 (2.75-9.87)	**69,8**	7 (2-18.4)

Lustbader & Lemp,1990	?	10	RxI + CS	graft, RxI 3 hours CS 2x3	Km	?	14.25	7.42	6.83	47,9	6-12
Frangieh et al,1991	P	7	RxI + CS	variable, CSx6	CAVK	?	10.89 ± 3.47 (8.25 - 18)	2.73 ± 1.97 (0.25 - 6)	8.16 ± 1.61 (2.5 - 16)	74.8	15.6 (9-19)
Fronterre & Portesani,1991	R	63 25	RxI RxI + CS	interface RxI 3 hours	P/ky	?	7.15 ± 1.67 12.56 ± 1.37	1.62 ± 0.84 2.88 ± 1.39	5.53 ± 1.44 9.68 ± 1.80	77,3 77	variable "
Kirkness et al,1991	R	21	RxI	interface, 2 hours	Refr.	2+	8.3	NA	3.6	43,4	12
	R	9	RxI + CS	1 x 2 CS	Refr.	2+	10.2	NA	4	39,2	12
Seitz & Naumann,1993	R	22	RxI+/-CS	variable	Km P/ky CAVK*	1	11.5 (7.25-20)	5.4 (1-11.25)	6.6 (0-13)	53	20.6 (6-60)
Whitehouse et al, 1994	R	33	RxI + CS	interface	Km Refr. P/ky	2	12.21 ± 3.59 (7-22.50)	3.93 ± 2.1 (0.50-8.75)		67,8	variable
Jacobi et al, 1994	R	25	RxI + CS	interface intraop km	intraop km	2	11.7 ± 4.9 (4.5-25)	6.2 ± 2.7 (2 - 15)	6.1 ± 4.3 (0.5-19)	47	24
Harto et al, 1996	R	8	RxI	graft nomogram	CAVK	1	10.70 ± 3.30 (6 - 15.5)	6.30 ± 2.90 (2 - 11)	4.40	45	2.7 yrs
Koffler & Smith, 1996	P	21	RxI + CS	graft	CAVK	?	5.2 (0.75-8.50)	3.0 (0-6.25)	2.2	56	?
Present study	P	16 15	RxI + CS	interface	CAVK Km/refr	5	8.00 ± 0.92 9.44 ± 0.84	4.24 ± 0.71 5.60 ± 0.51	3.76 ± 0.99 3.84 ± 0.70	47 40,7	12

* only 3 cases. R: retrospective, P: prospective, RxI: relaxing incision, CS: compression sutures, km: keratometry, Refr: refraction, P/ky: photokeratometry

Frangieh et al. (1991) were first to report their experience with surgery for post-PKP astigmatism guided by CAVK analysis. They used the technique of arcuate keratotomies combined with compression sutures in patients with more than 8 D astigmatism. The absolute scale was used to plan incision location and length, as well as the location of the suture placement in a similar fashion to our study. Five of the seven patients had improved postoperative BCVA of 1 line or more, and overall astigmatism was reduced by 74.8%. Although these results mark an improvement over those reported previously for surgery based on keratometry and keratoscopy information, other investigators (*Seitz & Naumann,* 1993; *Koffler & Smith,* 1996; *Harto et al,* 1996), as well as the present study, failed to reproduce similar net astigmatism reduction with the use of CAVK. Furthermore, in the present study the use of CAVK provided better results compared to the control group, but the difference was not significant for the majority of the astigmatic measurements. In particular, there was no significant effect to the net or vectorial reduction of astigmatism. This lack of significant difference between the two groups could be due to several reasons.

1) the numbers of patients presented here are relatively small and may not be truly representative of the different treatment groups. Indeed, power analysis calculations indicate that the minimum difference that the present study could detect was 2.6 D with an 80% power, or 3.00 D with a 90% power for a significant ($p<0.05$) variation. On the other hand, in order to detect a difference as small as 2.00 D with 90% chance, 35 eyes in each group are needed. This number of eyes is only likely to be collected in a multicentre study.

2) it was observed in the majority of cases, that the difference between plan 1 and plan 2 in group A was very small. The mean difference in the axis of the relaxing incisions was as small as 11 to 14 degrees for the two cuts. This is somehow surprising, but in view of the results in chapter 3 it should probably be expected. It has been shown previously in the thesis that regular astigmatic patterns are associated with high astigmatism. The present study population is highly

astigmatic (more than 4.00 D), and 71% of the eyes had regular astigmatism preoperatively, but only 29% of the eyes had irregular patterns. In contrast, a general post-PKP population is expected to show a reverse incidence of topographic patterns (regular to irregular ratio ~ 1:3 at 12 months post-PKP, *vide* chapter 3). CAVK has been used by *Maguire & Bourne* (1989b), to evaluate the reliability of preoperative keratoscope photographs to determine the proper axial placement of relaxing incisions. The authors came to a different conclusion than the present study. They found no preoperative corneal surface displayed a pattern of power distribution consistent with spherocylindrical optics. However their sample was only 4 eyes.

In view of the present study's findings, it is therefore possible that most of these eyes required symmetrical or almost symmetrical surgery and in that respect CAVK could not be proved extremely useful. In addition, the length of the relaxing incisions cannot be a precise duplication of what is seen on videokeratography, especially when differences in axes or incision lengths are as small as 10 degrees (1/3 of a clock hour cut). Despite that, such a minor rotation in the region of 10 - 15 degrees theoretically is expected to have quite an effect on the magnitude of astigmatic correction obtained when the intended axis and the actual axis are misaligned (*Stevens,* 1994).

3) another reason that may have influenced the results in this study, is that by pure chance (randomisation), 13 of the 15 patients allocated in group B (86.6%) had regular astigmatic patterns which would require symmetric surgery anyway. But it must also be emphasised that on the other hand, if anything, in this control group the surgical protocol followed (2 hours paired incisions for all eyes) would lead to undercorrection rather than overcorrection, if nomograms are to be believed.

4) finally, it is possible that factors other than the surgical design are more important in achieving better results after refractive surgery. In particular, perhaps variation in healing after the relaxing incisions is responsible for the residual

astigmatism. Clinicians have limited influence in the control of wound healing; topical corticosteroids may have some role (*vide* final discussion, chapter 6).

In addition, it has been shown here that following relaxing keratotomy, corneal topography tends to be more irregular. In both treatment groups, surgery produced less regular patterns and more irregular patterns. An ARVO poster presentation (*Vilchis et al,* 1995) came to the same conclusion.

Surgeon's experience was also found to have no significant effect on outcome. This is in agreement to a previous study by *Friedberg et al.* (1993) which indicated that radial and astigmatic keratotomies performed by beginning refractive surgeons under supervision (not on post-PKP eyes however), can be safe and effective with results comparable with those obtained by experienced refractive surgeons. Finally, the fact that 6/16 patients in group B compared to 2/16 patients in group A (a significant difference) experienced perforation as a result of refractive surgery could be anticipated to influence the results. Perforation evidences a very deep incision and this might well produce a better result in this group. Statistical analysis however rouled out intraoperative perforation as a significant factor to the outcome. It is possible that any potential beneficial effect of such deep incisions is lost by the use of the additional 11/0 sutures at the site of perforation to control the leak. Although great care was taken for these sutures to be placed without creating any tissue tension, this is technically very dificult.

Despite the moderate influence of CAVK in the final astigmatic results, before concluding on the findings of the study, it is important to understand it's limitations, mainly the relatively small number of eyes studied. The final answer to the questions of the study can only be given through a multicenter study.

5.6. Conclusions

Significant differences were not seen between the two treatment groups in:

- the amount of net astigmatism reduction (topographic, keratometric or refractive) by surgery.

- the amount of vector astigmatic change (91% for group A, 70% for group B).
- the amount of SAI, SRI change with surgery.

Significant differences between the two groups were seen only for:

- keratometric and refractive astigmatism at 12 months following refractive surgery, which was lower in group A than group B.

Refractive surgery was found to reduce regular astigmatic patterns incidence and respectively increase irregular patterns.
Minimal changes in the initial surgical plan were indicated by the use of CAVK, but this -as well as the non significance of the results-, may be related to the high incidence of regular astigmatic patterns encountered in the population of the present study.
A greater reduction in astigmatism was found to be associated with regular astigmatism (and also with OSBT and PSBT patterns). Previous refractive surgery was associated with worse results.
In summary, this study indicates that in terms of astigmatic correction, CAVK offers a limited advantage in designing refractive surgery after PKP, but this is likely due to the fact that most of these highly astigmatic corneas follow spherocylindrical optics with regular astigmatism (also shown in chapter 3).
However, in cases where irregular patterns are seen, they cannot be identified without the use of CAVK and in that respect CAVK is valuable. Whether in these particular cases the use of CAVK offers any significant advantage is not known. A prospective, multicentre, cohort study with big enough numbers of irregular astigmatic subjects should be conducted to answer this question. The suggestion however from the present study, is that a significantly greater surgical effect should be expected with regular (preoperatively) astigmatic patterns, irrespective of the treatment group. It seems that the biomechanics of corneas probably respond better in symmetric than in asymmetric surgery.

CHAPTER 6

FINAL DISCUSSION
AND
SUGGESTIONS FOR FURTHER WORK

This thesis dealt with some questions encountered with the use of computer assisted videokeratography. The introduction of these instruments in the recent years, has created great expectations. However, some weaknesses of a model of CAVK (TMS-1) used in the present studies were revealed in comparing it against the keratometer on highly astigmatic corneas, a field with lack of adequate published studies. A systematic bias of the TMS-1 towards the 10 SL/O Zeiss keratometer was found, in measuring steeper both principal meridians and higher amount of astigmatism consistently, not only for normal but also for post-PKP corneas. For highly astigmatic post-PKP corneas, the two instruments cannot be used interchangeably because their limits of agreement were found to be very broad not only for experimental, but also for clinical purposes. Repeatability of the TMS-1 was also found to be (a) observer related, and (b) astigmatism related. A novice observer showed a much larger variability in his measurements compared to the experienced examiner [Table 2.6]. Intraobserver variation with the TMS-1 is also astigmatism related, and increases with increasing magnitude of astigmatism. Higher deviation scores were observed in the plot diagrams for corneas with higher astigmatism [Figure 2.8B]. The repeatability of the TMS-1 on post-PKP corneas was poor (interobserver coefficients of repeatability: 1.88 D for steep meridian power, 3.86 D for flat meridian power, 4.06 D for astigmatism magnitude, 34° for astigmatic axis location). For the model used in the present studies (TMS-1), I think the focusing system plays a crucial role, and is probably responsible for the poorer results obtained with the novice observer. The near future will reveal whether new CAVK models with tracking systems, already commercially available, can provide better clinical or experimental results. In addition, in order for the CAVK to fulfil assumptions, the cornea must be positioned correctly and manufacturers should research for machines able to indicate when these assumptions are fulfilled or not. Algorithms based on tangential or instantaneous radius of curvature, rather than axial distance have also been developed and recently several manufacturers of CAVK have incorporated them. *Klein & Mandell* (1995) have compared different representations of corneal power and found that instantaneous power provides the most sensitive measure of local curvature changes, whereas the axial power gives an approximation of refractive power. Further prospective comparative studies are needed however, to answer the question of clinical importance of the new algorithms, as well as a general consensus among manufactures in terminology and topographic data presentation.

The second study presented here (chapter 3) dealt with the difficult problem of creating a clinically useful classification system for post-PKP corneas as previously proposed systems for normal corneas do not cover the spectrum of topographic patterns seen after PKP. Good interobserver agreement (a pre-requisite for clinical application) with a second examiner was achieved (91% after second review). Although it is generally believed that post-PKP is very often irregular, it was demonstrated here that regular and irregular astigmatic patterns are seen in about 2 to 1 ratio (59% vs. 30%) in postkeratoplasty corneas, with a trend for decreasing incidence of regular astigmatic patterns and corresponding increase of the irregular astigmatic patterns with time. In addition, regular astigmatic patterns as a pooled group were found to be associated with significantly greater mean topographic astigmatism than the pooled group of the irregular astigmatic patterns. If the proposed classification proves to be clinically useful, then there is a potential place in the future, of automatic pattern recognition with the use of artificial neural networks technology. A neural network model to interpret topographic patterns seen in corneal abnormalities, has already been used by *Maeda et al.* (1995) with promising results. Accuracy and specificity of the neural network was greater than 90%, with sensitivity ranging from 44% to 100%.

The next task of the studies (chapter 4), was to compare astigmatic results of two suturing techniques (SCAS vs. ICS). Postoperative refined astigmatic control and astigmatic comparisons were greatly facilitated with the use of CAVK. However, and despite a very careful protocol, only minimal astigmatic differences were seen between the two suturing groups. The main difference seen, was the earlier visual rehabilitation and earlier lowering of postoperative astigmatism with the SCAS group. This apparent advantage of the SCAS technique may just be a reflection of the earlier suture manipulation in this group, as compared with the 10th postoperative week that selective suture removal in the ICS group started. In view of these results, we may have to consider now earlier selective suture removal in ICS eyes. Some authors have advocated selective suture manipulation as early as 3 weeks post-PKP (*Binder*, 1985; *Burk et al*, 1988), but it is not known how soon may the first selective suture removal start without the risk of wound dehiscence.

The lack of significant astigmatic difference between the two groups is likely to be because suturing techniques can only partially modify the other factors that occur perioperatively such as trephination, or postoperatively (wound healing). Wound healing rates vary greatly between individual corneas, based on the intrinsic biomechanical properties of each cornea, the depth and pattern of the incision, the age and sex of the individual (*Eiferman et al*, 1992). We are not as yet able at present to control effectively this variability in wound healing. The only means that clinicians have are steroids. Although there are experimental studies with pharmacological agents (e.g. epidermal growth factor, proteoglycans, collagen) that can speed (or delay, accordingly) stromal wound healing after PKP, so far no such agent has been shown to be effective clinically. Further studies on the clinical application of these agents, and a better understanding of the fundamental properties underlying the corneal wound healing are needed. Most of the studies on normal wound healing have been carried out in the rabbit or cat, and these findings may not be applicable to human cornea (*Maurice*, 1987). Furthermore the rabbit is a poor model for studying keratotomy wounds because the rabbit cornea has no Bowman's layer and the healing in rabbits does not closely resemble that in humans (*Eiferman et al,* 1992).

Another finding of the chapter 4 study, was the increased complication rates seen with the single continuous suture. Nylon sutures biodegrade and may loosen. An ideal suturing material should be non reactive, resistant to biodegradation, but also with similar elasticity to nylon. The use of non-biodegradable sutures such as polyester (Dacron, Mersilene) or polypropylene (Prolene) has been advocated as these materials do not hydrolyze and remain intact for longer than nylon (*Frueh et al,* 1992a,1992b). However, Mersilene is not the answer for a running adjustable technique, as it has been shown that it shows low elasticity and tendency to break spontaneously when clamped with forceps (*Bertram et al,* 1990; *Filatov et al,* 1996). In addition, complications similar to the ones observed in the present study with nylon sutures, were observed with Mersilene (inadvertent breakage, cheesewiring, frequent extensive loosening, suture microabscesses) (*Bertram et al,* 1990; *Frueh et al,* 1992b). Finally, Mersilene sutures do not seem to give any better astigmatic results than nylon (*Ramselaar et al,* 1992).

The results of chapter 5 indicate that there is still much scope for improved predictability of refractive surgery with or without the use of CAVK. As with post-PKP astigmatism, the importance of variability in healing response may have been the major determinant of the outcome of refractive surgery. Apart from few histopathological studies in wound healing after radial keratotomy in humans (*Stainer et al,* 1982; *Maurice,* 1987; *Binder et al,* 1988), there is a lack of proper similar studies in post-RxI or post-PKP corneas that could help in understanding healing control better. Maybe substances that could be placed either in the keratotomy wound at the time of surgery, such as collagen plugs *(Waller et al,* 1996) or used topically in the immediate postoperative period could provide some control in wound healing. There are also some promising methods that have not as yet found clinical application but show a potential field for improvement. Wound strength in post-PKP corneas can be evaluated with holographic interferometry (*Calkins et al,* 1981), a method that has been used in industry for the past decades to detect structural defects in a number of products. Sharply demarcated fringe patterns outline structurally weak areas in the cornea, but this appears to be still technically very difficult to obtain.

Rastereography (such as PAR or Orbtech systems) may prove in the future to be advantageous to current Placido based CAVKs. This technology provides a real-time topographic information with accurate elevation measurements of the irregular regions of the cornea and would have several advantages (covering of the peripheral cornea up to the limbus, better in sudden topographic changes, etc.) for surgery performed at the mid-periphery of the cornea, as with relaxing incisions.

At the time of writing of this thesis, laser treatment of post-PKP irregular astigmatism has been tried in few studies (*Campos et al,* 1992; *Cheema et al,* 1995; *Gibralter & Trokel,* 1994; *Lazzaro et al,* 1996) with very few individuals. The early results however are not any better than conventional surgical treatment, and also PRK carries the disadvantage of substantial regression. This process is applied best in regular corneal astigmatism, but cannot adequately correct irregular astigmatic patterns. *Gibralter & Trokel* (1994) have described a technique of excimer laser ablations for irregular astigmatism that uses the information provided by CAVK maps, but their experience was presented with only two patients.

It still remains to be seen whether computer simulation to design refractive keratotomy procedures (*Bryant et al,* 1987; *Velinsky & Bryant,* 1992) has a place in clinical situations, especially in post-PKP corneas. At present, there are existing inabilities to determine the exact biomechanical coefficients of the living eye and particularly, to simulate the effect of corneal wound healing (*Hanna et al,* 1992).

Technical aspects of corneal manipulation have developed over the last twenty years. Further refinements in techniques are possibly unlikely to give great improvement in results. Similarly laser surgery can be very precise and predictable, but still give variable results in a percentage of patients. Probably the future for corneal surgery is linked to a better understanding of corneal wound healing and it's manipulation to give clinical advantage.

PUBLICATIONS DERIVED FROM THE WORK PRESENTED IN THIS THESIS

1. Karabatsas C, Cook SD, Figueiredo F, Diamond J, Easty DL (1993) : The role of corneal topography in the correction of high postkeratoplasty astigmatism. *Abstracts of International Conference on Cornea, Eye Banking and External Diseases.* Jerusalem; p.39

2. Karabatsas C, Cook SD, Easty DL (1993) : The efficacy of corneal topography in the surgical plan for correction of high postkeratoplasty astigmatism. *Proceedings of the 26th Panhellenic Ophthalmological Congress*; 236-239

3. Karabatsas C, Cook SD, Easty DL (1994) : Planning the surgical correction of high post-keratoplasty astigmatism: The use of corneal topography. *Invest Ophthalmol Vis Sci*; **35(4)**: 1880

4. Karabatsas CH, Easty DL (1996) : Cyanoacrylate glue treatment for persistent aqueous leak following relaxing incisions with compression sutures for high postkeratopalsty astigmatism. *Doc Ophthalmologica* **92**: 93-96

5. Karabatsas CH, Cook SD, Powell K, Turner P (1996a) : Agreement in measurements of irregular astigmatic corneas between keratometry and computer assisted videokeratoscopy. *Invest Ophthalmol Vis Sci*; **37(3)**: S563

6. Karabatsas CH, Hoh HB, Easty DL (1996b) : Epithelial downgrowth following penetrating keratoplasty with a running adjustable suture. *J Cataract Refract Surgery* **22**: 1242-1244

7. Karabatsas CH, Cook SD (1997) : Long-term follow-up of a single continuous adjustable suture in penetrating keratoplasty (letter). *Eye* **11**: 140-141

8. Karabatsas CH, Cook SD, Figueiredo FC, Easty DL (1997) : Is post-keratoplasty topographic pattern affected by the suturing technique? *Invest Ophthalmol Vis Sci*; **38(4)**: S938

9. Karabatsas CH, Hoh HB, Easty DL (1997) : Treatment of suture track leak (author's reply). *J Cataract Refract Surgery* **23**: 461-462

10. Karabatsas CH, Cook SD, Figueiredo FC, Easty DL (1997) : Complications related to suture manipulation during the first year following penetrating keratoplasty. *Proceedings of the XIth Congress of the European Society of Ophthalmology* **vol 2**: 1029-1033

11. Karabatsas CH, Hoh HB (1997) : Is it cataract or misalignment that affects corneal topography measurements? (letter) *J Cataract Refract Surgery* **23**: 694-695

12. Karabatsas CH, Cook SD, Powell K, Sparrow JM (1997) : Measurement agreement of keratometry and computer assisted videokeratography on postkeratoplasty corneas. *J Refract Surgery* (submitted)

13. Karabatsas CH, Cook SD, Sparrow JM (1997) : A proposed classification for topographic patterns seen after penetrating keratoplasty. *Arch Ophthalmol* (submitted)

14. Karabatsas CH, Cook SD, Papaefthymiou J, Turner P, Sparrow JM (1997) : Clinical evaluation of keratometry and computerised videokeratography: Intraobserver and interobserver variability on normal and astigmatic corneas. *Br J Ophthalmol* (submitted).

15. Karabatsas CH, Powell K, Papaefthymiou J (1997) : Measurement agreement of the 10 SL/O Zeiss keratometer and the TMS-1 computerised videokeratography on normeal corneas. *Ophthalmic Physiol Optics* (submitted).

16. Karabatsas CH (1997) : Management of postkeratoplasty astigmatism. *Eye News* (in press)

PRESENTATIONS AT MEETINGS

1. Corneal topography in the management of astigmatism
   Karabatsas C, Cook SD
   Bristol MedicoChirurgical Society Meeting. Bristol, December 1992 (poster presentation)

2. The efficacy of corneal topography in the surgical plan for correction of high postkeratoplasty astigmatism.
   Karabatsas C, Cook SD, Easty DL
   26th Panhellenic Ophthalmological Congress; Crete, Greece, May 20-23, 1993 (poster)

3. The role of corneal topography in the correction of high postkeratoplasty astigmatism.
   Karabatsas C, Cook SD, Figueiredo F, Diamond J, Easty DL
   International Conference on Cornea, Eye Banking and External Diseases. Jerusalem, June 20-24, 1993 (oral presentation)

4. The role of corneal topography in refractive surgery
   Karabatsas C, Cook SD
   South Western Ophthalmological Society Meeting, Bristol, June 1993 (oral presentation)

5. Planning the surgical correction of high post-keratoplasty astigmatism: The use of corneal topography.
   Karabatsas C, Cook SD, Easty DL
   ARVO annual meeting, Sarasota, Florida, USA, May 1-5, 1994 (poster presentation)

6. Surgical correction of postkeratoplasty astigmatism using corneal topographic imaging.
   Karabatsas C, Cook SD, Easty DL
   27th Panhellenic Ophthalmological Congress; Halkidiki, Greece, May 25-29, 1994 (oral presentation)

7. The management of postkeratoplasty astigmatism by two different surgical techniques. A prospective randomised study.
   Karabatsas CH, Cook SD, Figueiredo FC, Hoh HB, Diamond JP, Easty DL
   The Royal College of Ophthalmologists Annual Congress, Birmingham, May 22-25, 1995 (poster presenation)

8. Suturing techniques, postoperative management and long term astigmatic results in penetrating keratoplasty.
   Karabatsas CH, Cook SD, Figueiredo FC, Hoh HB, Easty DL
   28th Panhellenic Ophthalmological Congress; Athens, June 1-4, 1995 (oral presentation)

9. Auditing penetrating keratoplasty
   Cook SD, Karabatsas CH
   Sunderland Eye Hospital, September 15, 1995 (talk by invitation)

10. A proposed classification for topographic patterns after penetrating keratopalsty
    Karabatsas CH, Cook SD
    Oxford Ophthalmological Congress, Oxford, July 8-10, 1996 (poster presentation)

11. Aspects of anterior segment surgery
    Cook SD, Karabatsas CH, Sparrow JM
    Spring Ophthalmology Symposium of the Royal College of Physicians and Surgeons of Glasgow, Glasgow, February 26, 1997 (talk by invitation)

12. Is post-keratoplasty topographic pattern affected by the suturing technique?
    Karabatsas CH, Cook SD, Figueiredo FC, Easty DL
    ARVO annual meeting, Fort Lauderdale, Florida, USA, May 10-15, 1997 (oral presentation)

13. Complications related to suture manipulation during the first year following penetrating keratoplasty.
    Karabatsas CH, Cook SD, Figueiredo FC, Easty DL
    XIth Congress of the European Society of Ophthalmology, Budapest, June 1-5, 1997 (oral presentation)

14. The spectrum of corneal topography after keratoplasty: a proposed classification system.
    Karabatsas CH, Cook SD
    XIth Congress of the European Society of Ophthalmology, Budapest, June 1-5, 1997 (poster presentation)

15. Postkeratoplasty astigmatism. Causes, prevention, treatment
    Karabatsas CH
    Bath Royal United Hospitals, Bath, October 14, 1997 (talk by invitation)

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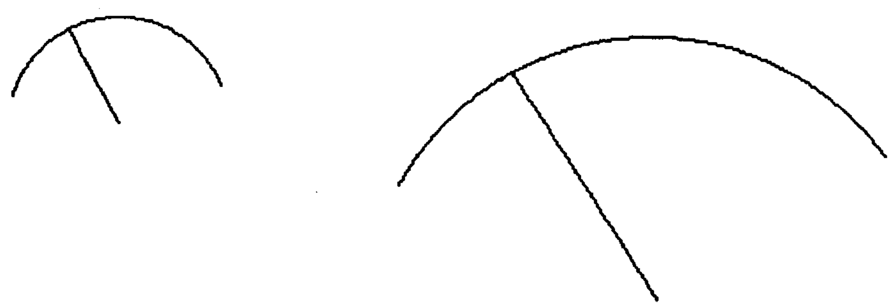
APPENDIX I

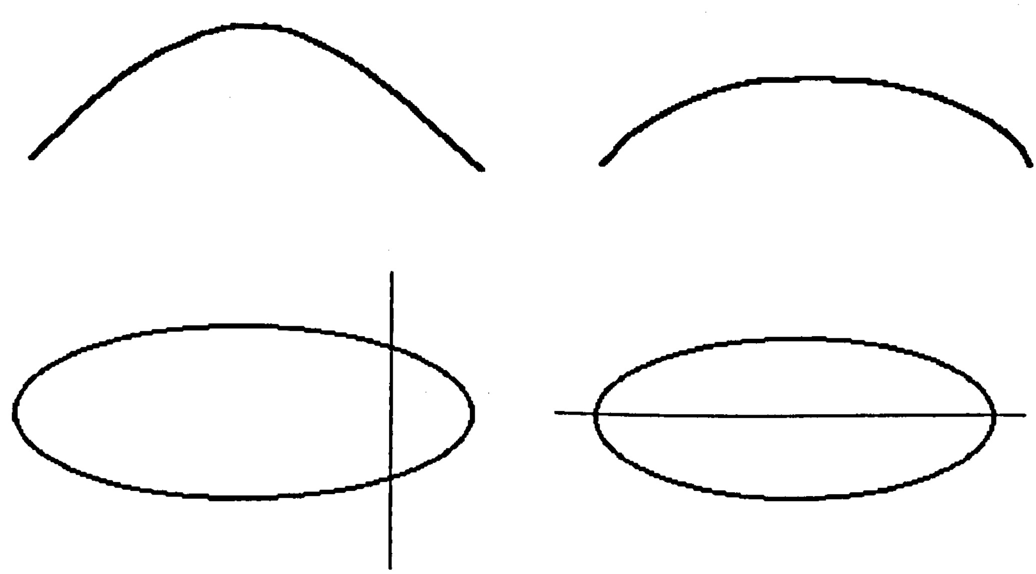
Terminology in describing corneal configuration [*Waring,* 1989a]

SPHERICAL CORNEA



Steeper	<u>Cornea</u>	Flatter
Shorter	<u>Radius of curvature</u>	Longer
Greater	<u>Dioptric power</u>	Smaller

ASPHERICAL CORNEA



Prolate ellipsoid	<u>Shape</u>	Oblate ellipsoid
Hyperbole	<u>Type of curve</u>	Parabola
Steeper to flatter	<u>Curvature from centre to periphery</u>	Flatter to steeper
Positive	<u>Shape factor</u>	Negative

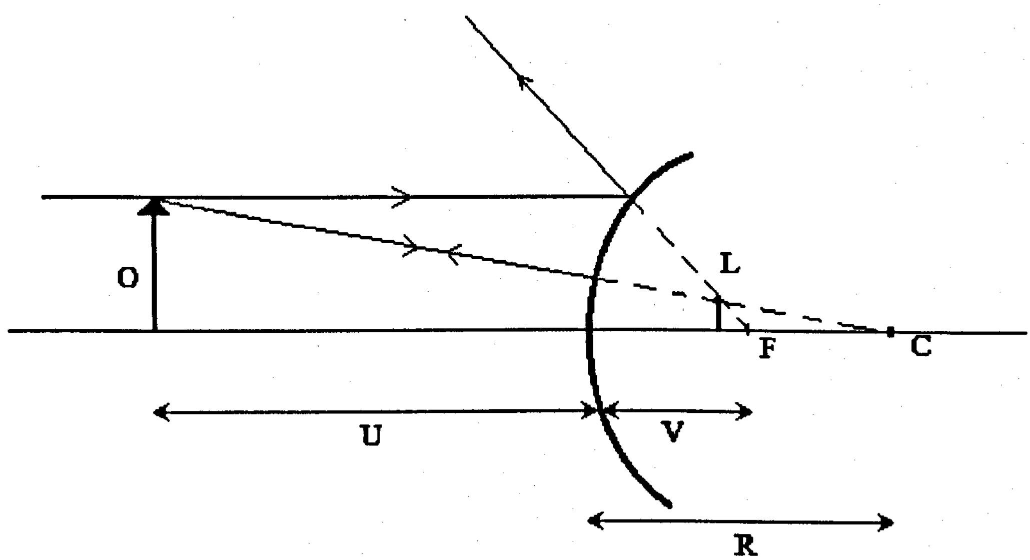
APPENDIX II

Terminology and mathematic equations for conicoidal surfaces

Term	Definition	Mathematical formula (*Baker, 1943*)
Conicoids	Surfaces that can be produced by rotating conic sections about a symmetry axis.	$y^2 = 2r_0x - px^2$
Ellipses	Curves, including the circle, that form a subset of the family of conicoids and are characterised by two independent parameters; a specific major axis and minor axis, or by a specific apical radius of curvature and eccentricity (*Mandell & St Helen,* 1971)	
	Ellipse with minor axis along x-axis	$p > 1$
	Circle	$p = 1$
	ellipse with minor axis along x-axis	$0 < p < 1$
Parabola	An ellipsoid with an *oblate* shape, that means flatter in the centre and steeper in the periphery; has a negative shape factor.	$p = 0$
Hyperbola	An ellipsoid with a *prolate* shape, steeper in the center and flatter in periphery, having a positive shape factor.	$p < 0$

APPENDIX III

Optical principle of keratometry



It is : L / O = V / U. In practice V = R/2, as the corneal image L is very closed to F.
Therefore L / O = R / 2U $\Rightarrow$ **R = 2U x L / O**

APPENDIX IV

Table
Equivalent Visual Acuity Measurements

Snellen Visual	**Acuity**		
6 Meters	**20 Feet**	**Decimal Fraction**	**LogMAR**
6/60	20/200	0.10	+ 1.0
6/48	20/160	0.125	+ 0.9
6/38	20/125	0.16	+ 0.8
6/30	20/100	0.20	+ 0.7
6/24	20/80	0.25	+ 0.6
6/20	20/63	0.32	+ 0.5
6/15	20/50	0.40	+ 0.4
6/12	20/40	0.50	+ 0.3
6/10	20/32	0.63	+ 0.2
6/7.5	20/25	0.80	+ 0.1
6/6	20/20	1.00	0.0
6/5	20/16	1.25	- 0.1
6/3.75	20/12.5	1.60	- 0.2
6/3	20/10	2.00	- 0.3

Adapted from *Ferris et al.* (1982)

APPENDIX V

Adapted from *Kaye et al.* (1992)

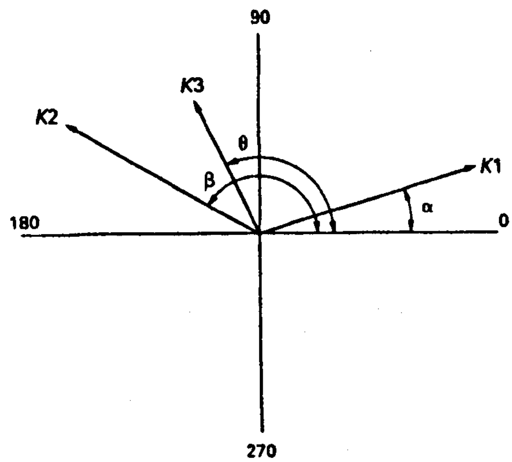


Figure 2 Representation of preoperative astigmatism, K1 at angle α, postoperative astigmatism, K3 at angle θ, due to the surgical effect, K2 at angle β.

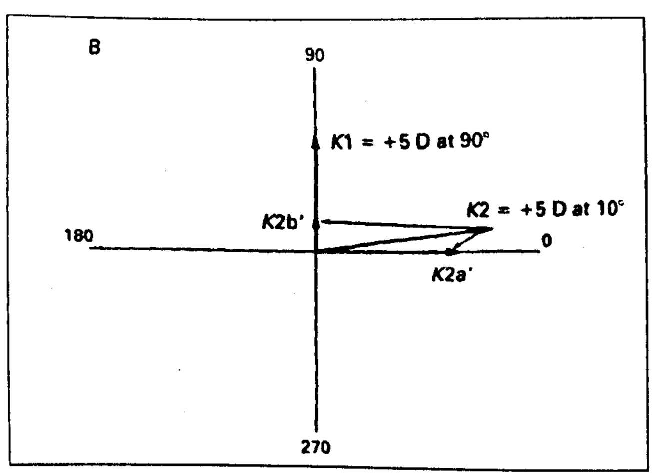


Figure 4B

CALCULATION OF *K2* AND *b*

$$K2^2=K1^2+K3^2-2.K1.K3.\cos 2(6-\alpha) \qquad (1)$$

K1 is the preoperative astigmatism at angle α,
K3 is the postoperative astigmatism at angle θ,
K2 is the surgically induced astigmatism or surgical effect at angle β, where

$$\sin 2\beta=(K3.\sin 2\theta-K1.\sin 2\alpha)/K2 \qquad (2)$$

From Figure 2,

$$K2=(K3\cos^2(\beta-\theta)-K1\cos^2(\beta-\alpha)-K3\sin^2(\beta-\theta)+K1\sin^2(\beta-\alpha))=K3\cos 2(\beta-\theta)-K1\cos 2(\beta-\alpha) \qquad (3)$$

where

$$2\beta=\arctan\{(K1\sin 2\alpha-K3\sin 2\theta)/(K1\cos 2\alpha-K3\cos 2\theta)\} \qquad (4)$$

If K2 is negative, conversion to a positive cylinder can be made as stated in the text, by adding or subtracting 90^o to or from β, if β is greater than or less than 0^o respectively. This can be verified by taking the second differential of K2 with respect to β - that is,

$$d^2K2/d\beta^2=-4K3\cos 2(\beta-\theta)+4K1\cos 2(\beta-\theta)=-4K2$$

Therefore, if K2 is negative, $d^2K2/d\beta^2$ is >0 and *K2* is a minimum for that value of β. Adding or subtracting 90^o from β, will make K2 positive and a maximum, as $d^2K2/db^2<0$.

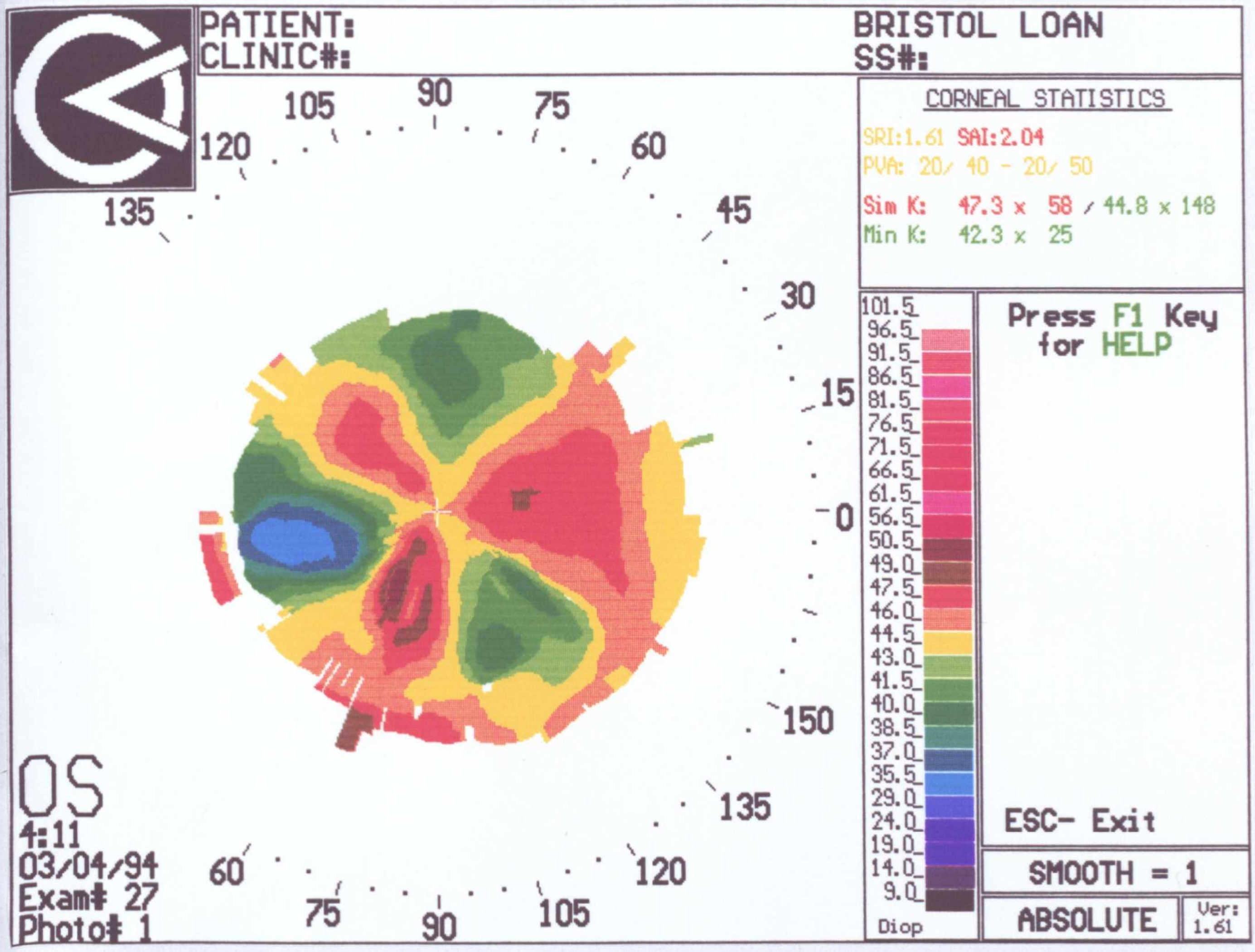
SURGICAL ACCURACY

From Figure 4B, the effectiveness of *K2* - that is, *K2', is K2'=K2a'-K2b'*

$$K2'=K2\cos^2(\beta-(\alpha+90))-K2\cos^2(\beta-\alpha)$$
$$=K2[\sin^2(\beta-\alpha)-\cos^2(\beta-\alpha)] \qquad (5)$$
$$=-K2\cos 2(\beta-\alpha)$$

Surgical accuracy (SA), can be defined as $SA=K2'/(K2+K3)$ (6)

APPENDIX VI



Example of a full size topographic map with colours of the absolute scale.